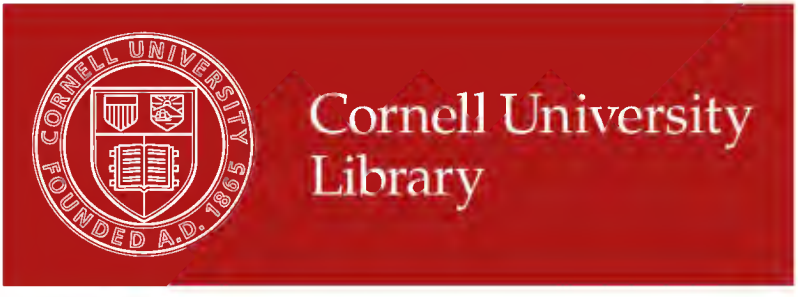

BACTERIOLOGICAL AND CLINICAL STUDIES

OF THE

DIARRHEAL DISEASES OF INFANCY

WITH REFERENCE TO THE

BACILLUS DYSENTERIÆ (SHIGA)

FROM

THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH

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INVESTIGATION OF 1903.

PREFATORY NOTE.

It was originally intended to include in this monograph only the papers relating to the work of the summer of 1903.

For the sake of completeness, however, it has seemed best to introduce also the papers of Duval and Bassett and of Knox covering observations made in the summer of 1902. The paper of Duval and Bassett has previously appeared only in abstract.

There has been added also the report of the observations of Wollstein upon the "Occurrence of the Bacillus Dysenteriae in Normal Infants." This work was undertaken subsequent to the findings of the summer of 1903.

THE EDITORS.

THE ETIOLOGY OF SUMMER DIARRHEA IN INFANTS.

(INVESTIGATION OF 1902.)

BY CHARLES W. DUVAL AND VICTOR H. BASSETT.

From the Laboratory of the Thomas Wilson Sanitarium, Baltimore.*

The successful studies of Japanese dysentery by Shiga in 1898, which led to the isolation of B. dysenteriae and its demonstration as the cause of acute endemic dysentery were followed by the studies of acute tropical dysentery in Manila by Flexner[1] in 1900 and epidemic dysentery in Germany by Kruse[2] in 1901 with results confirming the observations of Shiga. Since that time a considerable number of observations bearing upon and extending the studies just mentioned have been carried out both in the United States and elsewhere. Inasmuch as the organism has also been obtained from cases of dysentery in troops returning from China,[4] in Constantinople,[5] in Italy[6] and other European countries,[7] its wide diffusion in nature as well as its pathogenicity are clearly evident.

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*[A brief preliminary report of the results of this investigation was published in American Medicine, September 13, 1902, Vol. IV, p. 417. The present article and the following one by Dr. Knox, which contain the full reports, were ready for publication in October, 1902, and are here published in their original form. In consequence of the unfortunate delay in publication for which the authors are not responsible, later articles upon the same subject have been published without full knowledge of the detailed results obtained by Messrs. (now Drs.) Duval and Bassett in the summer of 1902, whose investigations at that time were the first to demonstrate an etiological relationship between the bacillus of dysentery and infantile summer diarrhea, and will remain of fundamental importance.—WM. H. WELCH.]

1. The Johns Hopkins Bulletin, February, 1900.
2. Deutsche med. Wochnschr., 1901, XXVII, 370.
3. Loc. cit.
4. Pfuhl, Veröffentlichungen auf dem Gebiete des Militär-Sanitatswesens, 1902, 65.
5. Deycke, Deutsche med. Wchnschr., 1901, XXVII, 10.
6. Celli. Personal communication and culture sent.
7. Th. Müller, Centralblätt für Bakteriol. u. Parasitenkunde, 1902, XXXI, 558. Rosenthal, Deutsche med. Wchnschr., 1903, XXIX, 97.

That the summer diarrheas of infants have an infectious origin has long been believed by clinicians and pathologists. Indeed, within the last ten or fifteen years notable contributions to the bacteriology of the dejecta, intestinal contents, and intestinal mucosa in the disease have been made by Escherich and his pupils in Germany and by Booker in this country. The valuable studies of these investigators have been less conclusive than might have been expected by reason of the multiplicity of bacteria in the intestine and the absence of satisfactory criteria of distinction between the saprophytic and parasitic varieties. Notwithstanding these drawbacks some facts have been established. But no success has attended the efforts to prove the action of a specific organism as the cause of infantile summer diarrheas. Indeed, no pathogenic organism was constantly present in the discharges.

The nomenclature of summer diarrhea is by no means clear. The various names given and the divergent views held as to its nature well illustrate the confusion that purely symptomatic and anatomical conceptions bring into the classification of disease.

The original problem set before us the past summer (1902), was the investigation of the intestinal bacteria of infants suffering from different forms of summer diarrhea, especially as to the presence of the Bacillus dysenteriae (Shiga). Subsequently, as a control, the stools of healthy infants were also studied. Following the method of investigation employed by Shiga in adult dysentery it was our intention to make use of the agglutination reaction of the blood of the patients with the organisms, in isolating the pathogenic organisms from the dejecta. Prof. Flexner drew our attention to this method of approaching the problem, and suggested the lines of special study.

The present unsatisfactory state of our knowledge of the etiology of the intestinal inflammations of children may be gathered from the statements regarding it to be found in any of the recent authoritative textbooks upon the diseases of children.

Methods of Studying the Dejecta.—On account of the admixture of microörganisms and the great capacity for multiplication in the intestinal contents of the colon bacilli, special methods should be resorted to in order to separate specific foreign microörganisms. The procedure employed by us in isolating B. dysenteriae from the stools was essentially that described by Vedder and Duval.[1] The stool is collected preferably upon a sterile gauze pad that is placed, in the usual manner, over the buttocks, previously cleansed with bichloride, etc., and over this

[1]Vedder and Duval: The Journal of Experimental Medicine, 1902, vi, 181.

the napkin is bound. The rectal tube may be employed, but it presents no special advantages over the former method. The stool should be examined immediately, if possible, and always without unavoidable delay, if successful and trustworthy bacteriological results are to be obtained.

Experience has taught that stools containing blood and mucus are especially favorable for isolating the bacillus of dysentery. One chooses by preference the bloody material which is suspended in sterile broth in quantity sufficient to give it a turbid appearance. As a rule about six loopfuls (*oese*) are used, and if several blood-flecked spots occur some is taken from each. When dealing with mucus rather than blood the same course is pursued, although sometimes three loopfuls suffice to render the bouillon (about 10 c.c.) cloudy. When bloody and mucous specks are distinguishable in the same stool one plates from each separately.

The number of plates prepared depends upon the character of the stool—whether fecal, mucous, or bloody. A large series of plates is prepared from muco-fecal matter and a smaller number from material containing much blood. The number of plates prepared from the different dejecta varied from 18 to 30. Of this series plates No. 1 and No. 4 were usually of little use, the first because of too heavy, the last of too light seeding. What is aimed at is to secure a large number of plates of Nos. 2 and 3, for subsequent study.

The dilutions are made in the usual way, after the settling of the coarser particles, by carrying 2, 4, 6, or 8 loopfuls of the suspension, depending upon its opacity, into a second bouillon tube (corresponding to agar plate No. 1 which is discarded) and from this bouillon into the melted agar tubes (2, 4, or 6) using in each the same number of loopfuls usually six (these forming plates No. 2) and from these the same number of loopfuls of agar suspension No. 2 are carried into No. 3 tubes (also 2, 4, or 6). A variation of this method of seeding, which insures a more certain distribution, is to carry about two loopfuls into one tube of agar, four into another, six into another, etc. What may be regarded as successful plates are those presenting about 25 to 200 superficial colonies. Thinly seeded plates, namely No. 4 plates, in all except very favorable and acute cases usually show only *B. coli.*

The most favorable material from which to isolate *B .dysenteriae* is obtained at autopsy, after opening the lower intestine with sterile instruments, by scraping the mucous membrane with a sterile knife; the scrapings being introduced into bouillon and used for plating as above described. We shall have occasion later to dwell upon the significance

of the fact that this organism is more abundant in the substance of the mucous membrane than in the intestinal contents, and is in far less danger of being overgrown *post mortem* in that location than in the dejecta.

The plates having been reversed, to avoid condensation upon the surface of the agar, are permitted to incubate at 37° C. for twenty-four hours. The first crop of colonies thus obtained having been marked off with a blue wax pencil, as described by Vedder and Duval, the plates are returned to the incubator for another twenty-four hours. This second crop of colonies is now examined and those presenting the characters of *B. dysenteriæ* (*vide infra*) are transplanted to glucose-agar. Incubation over night will suffice to separate all gas-forming from non-gas-forming varieties. Among the latter *B. dysenteriæ* is to be sought. While a certain number of dysentery colonies will appear within the first twenty-four hours the majority grow more slowly than those of *B. coli.* This fact is further emphasized by the occasional appearance of the former colonies as late as the fourth day of incubation of the plates. In some instances with positive blood reactions, in which colonies developing late were few in number and non-dysenteric in type, examination after some days of the plates marked off on the first day has yielded characteristic colonies, in small number, of the dysentery bacillus.

Physical Characteristics of Colonies of B. dysenteriæ on Agar-agar.—Inasmuch as no small part of the success of isolation of the bacillus of dysentery from stools, etc. depends upon the recognition of the colony and since agar-agar suffices for this distinction and possesses the important advantage of permitting rapid cultivation, a somewhat detailed description of the typical colonies upon this medium is given. The general cultural characters of the bacillus will not be described as this has already been done by Flexner[1] and by Vedder and Duval.[2]

We also noted that the reaction of the nutrient agar-agar is of prime importance; it should be *distinctly acid* to litmus. Should the reaction be neutral to litmus the difficulty of isolation of *B. dysenteriæ* is very much increased; and in the presence of an alkaline reaction isolation is rendered almost impossible. The reaction influences rapidity of growth, and perhaps, also, the type of colony. Alkalinity is a definitely inhibitory condition.

[1]Flexner: On the Etiology of Tropical Dysentery, Philadelphia Medical Journal, 1901, vi, 414; A Comparative Study of Dysenteric Bacilli, Univ. of Penna. Med. Bulletin, 1901, xiv, 190.

[2]Loc. cit.

When grown upon the acid medium the forms of the superficial colonies, which in age are not younger than 24 or older than 48 hours, are so distinctive that they can be recognized with much confidence. To this end the plates should be thinly spread and the layer of medium such as to insure a large proportion of superficial colonies.

With the naked eye the 24-hour colonies average 1 mm. in diameter and within the next 12 hours they add 0.5 mm. to their width. The 48-hour colony is about 2 mm. in diameter. At the expiration of 24 hours a well-defined nucleus can be detected, which remains stationary during the next 12 to 24 hours. The margin of the colony is uniform, regular, and unbroken, and gradually merges into the medium. The colony of 36 hours' growth shows already the zonular striation upon which we lay much stress, and this appearance persists almost or quite unchanged up to about 48 hours. The consistence varies with the age of the colony: at 24 hours the colonies are delicate and semi-translucent; at 48 hours they are more opaque, but still of considerable delicacy.

The former are bluish-white in color, the latter whiter, but even when viewed by reflected light do not exhibit a yellowish tint. The surface is not elevated perceptibly above the medium and the reflection is dull.

Under a magnification of ten times, the triple zone is strikingly evident. The nucleus of the 24-hour colony is regular in outline and unbroken, the granules of the middle zone are regular in size and appearance and equidistant from one another. At about 36 hours the nucleus begins to show irregularities; the periphery presents nodosities which a little later (48 hours) become separated and migrate towards the middle zone. The margin which is regular up to 36 hours begins now to assume a wavy outline which is persistent. The color is bluish by transmitted and brownish by reflected light.

Colonies older than 48 hours cannot be regarded as readily distinguishable from those of *B. coli.* After this period, the growth in thickness and opacity as well as in superficies entirely obliterates the characters upon which differentiation from *B. coli* can be made. As compared with colonies of the dysentery bacillus of 24 to 48 hours' growth, those of the colon bacillus of corresponding ages are larger, thicker, elevated, more opaque, and of yellowish hue. A nucleus is inconstant and the zonular striation wanting.

Record of Cases.—At the present time and, indeed, until such time as the etiology of the summer diarrheas is definitely established, it is desirable to combine the description of the bacteriological findings with certain important facts in the clinical history of the cases studied. For this reason we present here a brief report of the dejecta of the cases

examined; further reference to the clinical data will be found in the report of Dr. Knox.

Case I.—Irving. Infection occurred in the Sanitarium. First stool examined bacteriologically was semi-liquid, muco-fecal in character. Later specimen consisted almost wholly of mucus, flecked here and there with blood; still later there was muco-pus. Coverslips showed, besides leucocytes and red corpuscles, many bacilli of colon morphology and some cocci. Of 26 colonies transplanted to glucose-agar five developed no gas and proved later to be *B. dysenteriæ.*

Case II.—Williams. Movement semi-solid, muco-fecal. No blood or pus. Isolation of *B. dysenteriæ* positive. A second plating from this case gave identical results.

Case III.—Schuster. Stool semi-liquid, bloody, and muco-purulent. Result positive.

Case IV.—Schultz. Semi-solid, mucous stool; no blood or pus. *B. dysenteriæ* obtained in small numbers after several trials.

Case V.—Riall. Stool muco-fecal, greenish-brown in color. First trial negative. A few days later a small quantity of bloody mucus appeared in the stool; result positive. One week later a large mucous stool containing some firm white clumps and mucus streaked with blood was obtained. Separate suspensions into bouillon were made from the blood-stained and blood-free thin mucous flecks. From the former 30 colonies, from the latter two colonies of *B. dysenteriæ* were secured.

This case is of interest as illustrating the difficulties attending the study of the dejecta and as emphasizing the necessity for repeated examination before deciding upon a negative result. The first examination gave no dysentery bacilli, the second gave many, the third few, and the fourth none, all within a period of ten days.

Case VI.—Wolf. Semi-liquid, yellowish-brown, mucous stool; here and there small flecks of blood. Positive result; few colonies.

Case VII.—Friedman. Specimen contained much mucus and a few streaks of blood intermingled with fecal matter. Of 30 colonies subcultured into glucose-agar, nine gave *B. dysenteriæ.* Second specimen: very bloody mucous stool. Of 40 subcultured tubes, 37 consisted of *B. dysenteriæ.*

Case VIII.—Silk. First stool semi-solid and mucous; no blood. Very few dysentery colonies obtained. Second specimen contained muco-bloody patches; a large number of colonies were secured. The blood of this case agglutinated powerfully and retained this capacity for more than eight weeks (*vide infra*).

Case IX.—Hoffman. Small, liquid, non-fecal stool containing much bloody mucus and pus. From this material a high percentage of the organisms was obtained. A second stool was fecal with only a trace of mucus; no result. One week later blood again appeared in the stool when *B. dysenteriæ* was obtained from the plates prepared from the bloody but not from the purely mucous material. In this last examination ten new colonies appeared on the 48-hour plates, all of which proved to be *B. dysenteriæ.*

Case X.—Rabinowitz. First specimen small, containing viscid, greenish mucous lumps and purulent matter flecked with blood. Twenty-four hours later the stool was fecal and mucous. Two days later blood again appeared. In the first specimen dysentery bacilli were abundant; in the second, they were not

found; streptococci were present. This was a fatal case; autopsy not permitted. A rectal tube was, however, inserted and the mucosa of the colon scraped; from the scrapings *B. dysenteriæ* was obtained.

Case XI.—Pursley. Large, muco-fecal stool containing pus. Result positive; small number of colonies of *B. dysenteriæ* isolated.

Case XII.—Stevens. Semi-solid, muco-fecal specimen. Few colonies of dysentery bacillus; streptococci in moderate numbers. Two weeks later bloody streaks were observed on the napkin. From the bloody mucus a large number of colonies of *B. dysenteriæ* were obtained. This case terminated fatally and an autopsy was performed by Dr. Flexner. An abstract of the protocol, so far as it relates to the intestines, is as follows: The intestines are moderately distended and the large intestine is dilated and thickened. On opening the large intestine the entire colon is distended and the mucous membrane is thickened and covered with bloody mucus. Numerous punctiform hemorrhages and small ulcers extending through the mucosa are present in the large intestine, while the small intestine contains muco-sanguinolent contents, the mucosa showing punctiform hemorrhages but no ulcerations. The injected and hemorrhagic condition of the small intestine disappears at about the upper third of the jejunum.

Cultures gave *B. dysenteriæ* from the intestine, mesenteric glands, and liver. The greatest number of colonies was obtained from the scrapings of the mucous membrane; the next greatest number from the substance of the mesenteric gland of which a large part was transplanted.

Case XIII.—Mortensen. Semi-solid, greenish-yellow mucous specimen with little fecal matter and blood. Positive for *B. dysenteriæ.*

Case XIV.—Pittle. Abundant fluid stool with little fecal matter and some mucus; no blood. Small number of dysentery bacilli obtained.

Case XV.—Hicky. Small, thick, greenish, mucous stool containing blood and pus. Large number of colonies of *B. dysenteriæ.*

Case XVI.—Carr. Stool consisted almost entirely of pus and mucus with much blood. Regarded as a highly favorable specimen. Result positive. This case came to autopsy and the material obtained by scraping the mucosa yielded a much larger percentage of colonies of *B. dysenteriæ.* No streptococci were found.

Case XVII.—Lutz. First specimen dark, semi-liquid, containing mucus but no blood. One colony of *B. dysenteriae* secured. Second and third specimens (one week later) contained mucus and blood. From the third a number of colonies were obtained; streptococci present. Fourth specimen contained much blood; a large number of positive colonies secured. Sixth specimen: abundant muco-pus with little blood; positive but a smaller number of colonies of the dysentery bacillus found than in preceding specimen.

Case XVIII.—Heiland. Mucous stool with a little blood and fecal matter. Second stool almost wholly mucus and blood. Positive for *B. dysenteriæ.*

Case XIX.—Speckerman. Semi-solid, muco-fecal stool; no blood. Result positive for *B. dysenteriae.* The urine from the child was albuminous and cloudy; a bacilluria existed which was due to *B. coli.* A painstaking attempt to find *B. dysenteriæ* in the urine failed. The child died and the large intestine at autopsy showed enlargement of the solitary follicles with pitting of their centres and surrounding deep congestion; no definite ulceration was present. Scrapings from the mucosa gave a high percentage of colonies of *B. dysenteriæ.*

Case XX.—Lavine. Abundant, greenish, mucous stool; no fecal matter. Small number of colonies of dysentery bacillus.

Case XXI.—Love. Thick, yellowish-green stool showing blood-stained mucus. From the plates *B. coli, B. proteus* and *B. dysenteriæ* isolated. All tested with patient's blood and only the last reacted positively.

Case XXII.—Proser. The specimen examined consisted of a muco-fecal stool containing a few flecks of blood. The result was positive. This child died later, but an autopsy was not permitted. However, by passing the rectal tube and scraping the mucosa a small quantity of blood-stained material was secured from which *B. dysenteriæ* was obtained.

Case XXIII.—Walsh. In the abundant mucous stool a few small collections of pus cells occurred; result positive. Some twelve days later a second examination of a semi-fluid, muco-fecal stool was made with negative results. The child died five days after the second examination and an autopsy was made eight hours after death. The lymphatic nodes of the cecum were swollen and the mucosa over them pitted; the mucosa of the transverse colon showed numerous small, round ulcers occurring as pits in the enlarged solitary nodes; the mucosa of the descending colon was thickened but intact. The contents of the large intestine were muco-pus, blood being absent.

The bacteriological examination gave *B. coli, B. lactis aerogenes, Streptococcus pyogenes,* and *B. dysenteriæ;* the last was obtained from the intestine only; the others from additional organs, such as the liver and mesenteric glands. This case was instructive in that on some of the plates *B. dysenteriæ* came out very late.

Case XXIV.—O'Donnell. The specimen examined had a bad odor, consisted chiefly of feces and mucus and showed a few patches of blood-stained mucus. Using the bloody areas ten of the twelve transplantations to glucose agar proved to be *B. dysenteriæ.* The next stool contained more blood; 27 out of 28 transplants were dysentery bacilli.

Case XXV.—Rea. Stool muco-fecal; no blood. Eight of 30 tubes transplanted positive for *B. dysenteriæ.* It is to be noted that the blood in this case failed to give the agglutination test, although tried several times.

Case XXVI.—Tucker. Small greenish, purulent, blood-flecked stool. Several examinations were required to discover the organism, which was finally found in very small numbers.

Case XXVII.—Golman. The first stool was chiefly fecal; very few dysentery bacilli. The second stool examined three days later was muco-purulent and contained blood. Many dysentery bacilli found. A third stool gave good results. The child died and an autopsy was refused. The mucosa of the lower gut was curetted and from this material many colonies of *B. dysenteriæ* developed. The plates in this case contained many colonies of a bacillus which agreed culturally with *B. pyocyaneus.*

Case XXVIII.—Stevens. Stools contained mucus, but little blood. Results were positive in 26 of the 37 glucose-agar tubes inoculated.

Case XXIX.—Macomber. Specimen abundant, greenish, showing mucus and some purulent foci and bloody mottling. Results positive for dysentery bacilli which were present in large numbers.

Case XXX.—Gerhardt. Muco-fecal stool without blood. Of 36 colonies transplanted, 14 proved to be *B. dysenteriæ.*

Case XXXI.—Lubinsky. Semi-solid fecal stool with a foul odor. No blood present. Of a large series of transplantations to glucose-agar three tubes of *B. dysenteriæ* were recovered.

Case XXXII.—Jackson. Very small mucous stool containing no blood and little fecal matter. A small number of dysentery bacilli were recovered.

Case XXXIII.—Hoffman. Stool large, muco-purulent and blood-stained. *B. dysenteriæ* present.

Case XXXIV.—Hirste. Muco-fecal stool; no blood. Small number of colonies of dysentery bacillus.

Case XXXV.—Plater. Specimen muco-fecal with few spots of blood. Of 49 subcultures 30 were *B. dysenteriæ.*

Case XXXVI.—Dukehardt. This case is given in some detail in order to show the difficulties that sometimes attend the isolation of *B. dysenteriæ.* The first stools examined were scanty, viscid, whitish, and contained mucus; blood was absent. From two stools eight plates were made. A small number of new colonies developed on the second day. These were streptococci. Seventy subcultures were made from the new and from suspicious looking old colonies. The bacillus of dysentery was not obtained; the organisms transplanted were streptococci, *B. coli,* and an undetermined bacillus which failed to react to the serum of the patient. Five days later cultures were taken from some slightly bloody mucus obtained by gently scraping the rectal mucosa through a proctoscope. Of 100 colonies subcultured only four proved to be *B. dysenteriæ,* the rest consisting of streptococci and *B. cali.*

Case XXXVIII.—Bogatsky. Muco-fecal stool; no blood. Small number of colonies of *B. dysenteriæ* developed.

Case XXXIX.—Triebosky. No stool was obtained from this case; but scrapings from the intestinal mucosa gave a small number of colonies of *B. dysenteriæ.*

Case XL.—Stabler. Scanty, liquid, muco-fecal stool; no blood. The plates from this case contained streptococci in predominating numbers; the bacillus of dysentery was recovered in small numbers only.

Case XLI.—Out-patient. Stool secured with rectal tube. The specimen was dark green and liquid; no blood or mucus. Twenty plates were made; of these one is worthy of special description since at the end of twenty-four hours only seven colonies had appeared. These were marked and later determined to consist of *B. cali. Upon examining this plate 24 hours later over 200 new superficial colonies had appeared. All these proved to be B. dysenteriae.*

Case XLII.—Out-patient. The blood of this patient had been tested in advance with positive results on the fifth day of the disease. Stool obtained with the rectal tube consisted chiefly of mucus with here and there bloody flecks; a moderate number of *B. dysenteriæ* present.

The foregoing list comprises the records of 42 cases of infantile diarrhea in which the bacillus of dysentery was found. The total number of cases examined for dysentery bacilli was 53; in 11 cases negative results were obtained although in all the fresh stools were studied. Of the 11 negative cases, 2 were fatal but autopsies could not be secured; in 3 cases a definite history of entero-colitis of some

weeks' standing was obtained. The stools were muco-purulent but did not show any blood. In only one had blood been observed by the mother at the beginning of the illness. Among the remaining were cases of so called "dyspeptic diarrhea."

After obtaining so many positive results in cases of suspected infection we undertook the study of the stools of 25 infants consecutively without reference to the form of the disease as inferred from the clinical symptoms. We succeeded in recovering B. dysenteriae in 19 cases. Of the 6 cases 3 were examples of simple marasmus; one a case of chronic entero-colitis in which blood had been noted in the stool a month or more before; and the remaining 2 were of the so-called catarrhal enteritis, with fluid stools but without blood.

A Study of Stools of Normal Children.—This undertaking did not afford much hope of success even if the bacilli were present in small numbers. Our experience in the examination of fecal stools even when mixed with mucus had shown the great difficulty in isolating this organism, when it was greatly outnumbered by the colon bacilli. Until some useful enriching method for *B. dysenteriæ* in mixtures with other organisms is found negative results cannot be regarded as conclusive.

We subjected to careful examination the stools of 25 infants ranging in age from seven days to two years, who had never been ill with intestinal disease. The dejecta were collected on sterile pads and plated immediately. The series can be divided into two classes:

Class I.—Infants one week to six months old. Stools yellowish-brown, homogeneous, fecal; no mucus, blood or pus present. Under the microscope moderate numbers of bacilli and cocci found.

Class II.—Older children. Stools large, semi-solid, fairly homogeneous. Color brownish-green or gray. Odor offensive. The microscopical examination did not differ from that of the first class.

The same method of bacteriological study was pursued as with the sick children, but in no instance was any microorganism obtained in cultures that corresponded to the *B. dysenteriæ.* The flora, so far as studied by us, consisted of *B. coli, B. lactis aërogenes, B. proteus,* and *Streptococcus pyogenes.*

An agglutination test, intended to be confirmatory only, was made with the blood of these children (1) with the organisms obtained from their stools, and (2) with *B. dysenteriæ.* Only negative results were obtained.

The Agglutination Reaction.—We look upon the agglutination reaction as of great importance in the study of this disease. After the experience gained by one of us (Duval) in the application of the re-

action to the study of the dysentery of adults and in view of the results of the present investigation we are inclined to rank its value along with that of the Gruber-Widal test in typhoid fever.

The technique of the reaction cannot be disregarded. We are convinced that by care in its application early cases and cases of mild infection can be detected. When the agglutinative value of the blood is high no special difficulty presents itself. But when small quantities of agglutinin are present in the blood a proper ratio between the quantity of serum and the number of bacteria must not be neglected if trustworthy results are to be expected.

The suspension of bacteria for the test is obtained from agar-agar slants which have been incubated for from 12 to 24 hours. Older cultures and growths upon other media are less useful. One standard loop

TABLE I.

INFLUENCE OF RATIO BETWEEN QUANTITY OF SERUM AND NUMBER OF BACTERIA UPON AGGLUTINATION REACTION.

Organism.	Case from which Organism Was Secured.	Case from which Blood Was Taken.	Dilution.	1 Hour.	Reaction Final.	Seeding.
B. dysent.	Harris	Bedford	1-20	—	—	Heavy.
B. dysent.	Harris	Bedford	1-20	+	+	Light.
B. dysent.	Harris	Bedford	1-50	—	—	Light.
B. dysent.	Schuster	Bedford	1-20	—	—	Heavy.
B. dysent.	Schuster	Bedford	1-20	+	+	Light.
B. dysent.	Schuster	Bedford	1-50	—	—	Light.
B. dysent.	Harris	McDonnell	1-20	—	Sug.	Heavy.
B. dysent.	Harris	McDonnell	1-20	+	+	Light.
B. dysent.	Harris	McDonnell	1-50	—	—	Light.
B. dysent.	Schuster	McDonnell	1-20	—	—	Heavy.
B. dysent.	Schuster	McDonnell	1-20	+	+	Light.
B. dysent.	Schuster	McDonnell	1-50	—	—	Light.
B. dysent.	Harris	Stabler	1-20	—	—	Heavy.
B. dysent.	Harris	Stabler	1-20	+	+	Light.
B. dysent.	Harris	Stabler	1-50	—	—	Light.
B. dysent.	Schuster	Dukehardt	1-20	—	Sug.	Heavy.
B. dysent.	Schuster	Dukehardt	1-20	+	+	Light.
B. dysent.	Schuster	Dukehardt	1-50	—	—	Light.
B. dysent.	Harris	Wolfe	1-16	Sug.	+	Heavy.
B. dysent.	Schuster	Wolfe	1-16	+	+	Light.
B. typhi. (control)		Wolfe	1-16	—	—	Light.

+ =positive; — =negative; Sug. =suggestive. "Harris" is a culture from the Philippines and was obtained from one of the original cases investigated by Flexner. "Schuster" is Case III in our series.

(*oese*) of surface growth should be suspended in a tube (8-10 c.c.) of clear bouillon. The inoculated bouillon is placed in the thermostat for from 15 minutes to one hour, or until a distinct but faint diffuse clouding of the fluid is noticeable. The blood is drawn into suitable tubes from which the clear serum can be separated. The dilutions are made in the usual way with graduated pipettes.

The seeding of the bouillon should be controlled. We found the best results to come from that seeding which, when bacterial suspension and diluted serum were mixed, showed about a dozen bacilli to the microscopic field. We wish to lay especial emphasis upon light seeding and strongly urge that no bacterial suspension be considered suitable unless it fulfils this requirement. The rule which can be given is somewhat as follows: serum in low dilutions may be more heavily seeded than in high ones, and powerful bloods more than weak ones. There seems to be a fixed relation between the amount of agglutinating substance and the number of organisms with which it will react. This is shown in Table No. 1.

The first effect of positive sera is to bring about a cessation of the indeterminate vibration (Brownian movement) of the bacilli. In the completed reaction, in spite of the light seeding, large clumps of bacilli result. In a certain number of cases the clumps, instead of being compact, show the loose skein arrangement described by Pfaundler with typhoid bacilli, and noted with *B. dysenteriæ* by Flexner and by Kruse. The clumps may remain stationary, if evaporation is prevented, for from 24 to 72 hours; or a diffuse growth through the fluid or even disintegration of bacilli (bacteriolysis) may take place.

We do not lay great stress upon the time factor which, with our present imperfect knowledge, cannot at best afford more than an empirical rule. Bloods of high power in low dilution begin to react in a few minutes, the reaction being complete in from one-half to one hour. Still other and quite powerful specimens may require from 2 to 3 hours; and definite reactions may occasionally be as late as eight hours in appearing.

The onset and duration of the reactions could be studied in a small group of cases. Of 13 children tested during the first week of illness ten gave positive and three negative results. One case reacted on the second and one each on the third, fourth and fifth days. Two cases reacted on the sixth, four on the seventh, and one on the eighth day. Of six children tested in the second week one was positive on the eighth day, one each on the tenth and fourteenth days; the others remaining negative or reacting later. Of ten children tested in

TABLE II.

DURATION AND VARIATION OF AGGLUTINATION REACTION WITH BLOOD-SERA FROM CASES OF SUMMER DIARRHEA.

Case Number.	Day of Disease.	Blood.	Dilution.	Source of Bacilli.	Results.		Remarks.
					1 hr.	Final.	
18	23	Heiland	1-16	Heiland	—	—	Duration of acute stage of disease was five weeks.
		Heiland	1-16	Philippine	—	—	
		Heiland	1-16	B. typhi	—	—	
	30	Heiland	1-500	Heiland	+	+	
		Heiland	1-500	Philippine	+	+	
		Heiland	1-16	B. typhi	—	—	
		Heiland	1-16	B. coli	—	—	
	57	Heiland	1-50	Heiland	+	+	
		Heiland	1-200	Heiland	—	—	Case well on sixty-first day.
	64	Heiland	1-16	Heiland	—	—	
9	3	Hoffman	1-16	Hoffman	—	—	Duration four weeks.
	6	Hoffman	1-50	Hoffman	+	+	
	10	Hoffman	1-16	Hoffman	—	—	
		Hoffman	1-16	Philippine	—	—	
8	10	Silk	1-1,000	Silk	+	+	
	67	Silk	1-200	Silk	Sug.	+	
		Silk	1-200	Philippine	Sug.	+	
		Silk	1-300	Silk	—	—	
		Silk	1-16	Silk	—	—	
7	5	Friedman	1-16	Friedman	—	—	Improved on 19th day. Blood never reacted in high dilution.
		Friedman	1-16	Flexner	—	—	
	8	Friedman	1-16	Friedman	+	+	
		Friedman	1-16	Philippine	+	+	
	10	Friedman	1-50	Friedman	+	+	
		Friedman	1-50	Philippine	+	+	
		Friedman	1-16	B. typhi	—	—	
	19	Friedman	1-16	Friedman	—	—	
6	8	Wolfe	1-16	Wolfe	—	—	Duration of acute stage was about three weeks. Relapse on 50th day. Well in 10th week.
	17	Wolfe	1-40	Wolfe	+	+	
		Wolfe	1-16	B. typhi	—	—	
	17	Wolfe	1-16	Wolfe	+	+	
	68	Wolfe	1-16	Wolfe	+	+	
	72	Wolfe	1-16	Wolfe	—	—	
Out-patient	2	Syracuse	1-25	Flexner	+	+	This is a blood sent to us from a case of summer diarrhea in Syracuse.
		Syracuse	1-25	Silk	+	+	
		Syracuse	1-50	Philippine	—	Sug.	
		Syracuse	1-100	Philippine	—	—	
	8	Syracuse	1-250	Philippine	+	+	
		Syracuse	1-300	Philippine	—	—	
	16	Syracuse	1-100	Philippine	+	+	
		Syracuse	1-150	Philippine	—	—	

* "Philippine" is the Harris organism referred to in Table I.

the third week, two reacted on the fifteenth, two on the sixteenth, one on the seventeenth, two on the nineteenth, and one on the twenty-first day. One child giving a negative reaction on the sixteenth day gave a positive one two days later. Table No. II gives the data as to the variation and duration of the reactions.

The agglutination reaction is, therefore, seen to appear early and may be looked for with considerable confidence at the end of the first week of illness. A small number of the children failed to react until much later and in some cases there was no reaction.

Our present knowledge leads us to think that, although the reaction of agglutination is persistent, it is sometimes lost or greatly reduced during convalescence. If death take place late in the disease the agglutinative power of the blood has also suffered diminution. On the other hand, chronic cases have still given good reaction as late as the third or fourth month of the disease.

TABLE III.

REACTION OF "SILK" BACILLUS TO BLOOD OF CASES OF SUMMER DIARRHEA.

Organism.	Blood.	Dilution.	Result; One Hour.
Silk	Silk	1-1,000	+
Silk	Wiegand	1-25	+
Silk	Carr	1-400	+
Silk	Yerzak	1-50	+
Silk	Rabinowitz	1-1,000	+
Silk	Siegal	1-20	+
Silk	Friedman	1-50	+
Silk	Tucker	1-100	+
Silk	Golman	1-100	+
Silk	Lavine	1-25	+
Silk	Love	1-50	+
Silk	Proser	1-20	+
Silk	Wheeler	1-20	+
Silk	Brown	1-60	+
Silk	Breitbach	1-200	+
Silk	Macomber	1-200	+
Silk	Walsh	1-100	+
Silk	Stevens	1-100	+
Silk	Plater	1-160	+
Silk	Wolf	1-40	+
Silk	Mortenson	1-25	+
Silk	Heiland	1-1,000	+
Silk	C———	1-1,000	+
Silk	Speckerman	1-100	+
Silk	Bogatsky	1-16	+
Silk	Triebasky	1-50	+
Silk	Bradley	1-100	+
Silk	Lucas	1-100	+
Silk	Bauch	1-100	+
Silk	H———	1-100	+
Silk	Stabler	1-25	+
Silk	Lorber	1-25	+
Silk	Dukehardt	1-25	+

The matter of cross-reactions also engaged our attention. We think this important in respect to the question of identity of species of the organisms with which we are working. Our opportunities to pursue this study were good. In the first place organisms from several distant localities were available—Japan, the Philippine Islands, the United States. The last included bacilli obtained both from adult dysentery and summer diarrheas. Besides many different specimens of blood

TABLE IV.

AGGLUTINATION REACTIONS OF MT. WILSON ISOLATIONS WITH ANTI-DYSENTERIC SERUM.

Isolations.	Dilution.	Results.	
		One Hour.	Final.
Schuster	1-500	+	+
Silk	1-1,000	Sug.	+
Friedman	1-200	+	+
Riall	1-400	+	+
Hoffman	1-100	+	+
Williams	1-100	+	+
Wolfe	1-100	+	+
Schmelz	1-500	+	+
Mortenson	1-500	+	+
Carr	1-500	+	+
Hickey	1-500	+	+
Rabinowitz	1-1,000	+	+
Heiland	1-200	+	+
Irving	1-200	+	+
Love	1-200	+	+
O'Donnell	1-200	+	+
Boeckerman	1-500	+	+
Walsh	1-500	+	+
Proser	1-500	+	+
Macomber	1-500	+	+
Golman	1-500	+	+
Plater	1-500	+	+
Jackson	1-500	+	+
Stevens	1-500	+	+
Bogatsky	1-500	+	+
Triebasky	1-500	+	+
Lutz	1-500	+	+
Pittle	1-500	+	+
Pursley	1-500	+	+
Tucker	1-500	+	+
Rea	1-500	+	+
Geyhardt	1-500	+	+
Lavins	1-200	+	+
Lubinsky	1-200	+	+
Marcus	1-200	+	+
Hirste	1-200	+	+
Dukehardt	1-500	+	+
Stabler	1-100	+	+
P——— (outside case)	1-200	+	+
H——— (outside case)	1-100	+	+
Hoffman (301)	1-400	+	+
Stevens (185)	1-200	+	+

With dilutions 1-50 or less, positive reactions were obtained in from 10 to 30 minutes.

which could be secured from children, anti-dysenteric serum obtained by Gay from immunized horses was always available. For the purpose of completeness a strain of *B. typhosus* was carried along with the other bacilli, but no further mention of it need be made as it always behaved negatively. Table III gives the reactions obtained with

TABLE V.

SHOWING THE AGGLUTINATION REACTION OF BLOOD OF SICK CHILDREN WITH THE DYSENTERIAE ISOLATED FROM CASES OF ACUTE DYSENTERY.

Suspension of Bacilli.	Blood.	Dilution.	Results.	
			One Hour.	Final.
Shiga (Japan)	Lavine	1-25	+	+
Flexner-(Harris) (Philippine)	Lavine	1-50	+	+
Vedder and Duval (New Haven)	Lavine	1-50	+	+
Kruse (Germany)	Lavine	1-50	+	+
Flexner-(Harris)	Wiegand	1-40	+	+
Flexner-(Harris)	Schuster	1-200	+	+
Flexner-(Harris)	Pursley	1-50	+	+
Flexner-(Harris)	Friedman	1-25	+	+
Flexner-(Harris)	Stevens	1-16	+	+
Flexner-(Harris)	Silk	1-1,000	+	+
Flexner-(Harris)	Wolfe	1-25	+	+
Flexner-(Harris)	Carr	1-50	+	+
Flexner-(Harris)	Mortensen	1-16	+	+
Flexner-(Harris)	Yerzak	1-50	+	+
Flexner-(Harris)	Hieland	1-50	+	+
Flexner-(Harris)	Proser	1-25	+	+
Flexner-(Harris)	Wheeler	1-20	+	+
Flexner-(Harris)	Love	1-20	+	+
Flexner-(Harris)	Brown (outside case)	1-60	+	+
Flexner-(Harris)	Rea	1-16	+	+
Flexner-(Harris)	Walsh	1-100	+	+
Flexner-(Harris)	Macomber	1-50	+	+
Flexner-(Harris)	Franklin	1-16	+	+
Flexner-(Harris)	Tucker	1-100	+	+
Flexner-(Harris)	Golman	1-100	+	+
Flexner-(Harris)	Siegal	1-20	+	+
Flexner-(Harris)	Gordon	1-16	+	+
Flexner-(Harris)	Marcus	1-16	+	+
Flexner-(Harris)	Hirste	1-16	+	+
Flexner-(Harris)	Rabinowitz	1-500	+	+
Flexner-(Harris)	Irving	1-200	+	+
Flexner-(Harris)	Breitbach (outside case)	1-200	+	+
Flexner-(Harris)	C——— (outside case)	1-1,000	+	+
Flexner-(Harris)	Burns	1-50	+	+
Flexner-(Harris)	H——— (outside case)	1-50	+	+
Flexner-(Harris)	Bedford	1-20	+	+
Flexner-(Harris)	Stabler	1-25	+	+
Flexner-(Harris)	Dukehardt	1-25	+	+
Flexner-(Harris)	Lorber	1-25	+	+
Flexner-(Harris)	Bogatsky	1-25	+	+
Flexner-(Harris)	Boehm	1-16	+	+
Flexner-(Harris)	Syracuse (outside case)	1-250	+	+

Note:—B. typhosus used as control was negative in 1-16 dilutions.

the bacillus from "Silk" child (Case VIII) towards a number of blood sera from cases of summer diarrhea. Table IV gives the reactions with anti-dysenteric serum and the bacilli isolated from the Mount Wilson cases of summer diarrhea. Table V shows the cross-reactions between the blood of the sick children and the bacilli obtained from cases of acute dysentery chiefly in adults. The interactions of sera and bacilli from many sources is clearly shown.

We also studied the agglutination of *B. coli*, isolated from stools, with the sera of children ill with diarrhea. Our results can be stated briefly. In a fair number of cases the sera reacted positively with the particular variety of colon bacillus isolated from a given case but usually only in dilutions of 1:16. In two instances only out of 50 cases were reactions obtained in 1:25 dilutions. Cross reactions were never secured.

Is the bacillus of dysentery motile in artificial cultivation? The difference of view expressed by Shiga and Flexner on the one hand, and Kruse and Martini and Lentz[1] upon the other, makes it desirable to add another word upon the question under dispute, especially as we have been successful in devising a method through which it is possible to develop motility in the several varieties of bacilli now known. Shiga from the beginning of his studies claimed motility for his bacillus, and Flexner described locomotion in the bacilli isolated by him in the Philippines although it was not afterwards detected by him in his artificial cultivations. Vedder and Duval failed to discover motility in the bacilli obtained by them from cases of acute dysentery studied in this country, while, through a modification of Van Ermengem's method, they succeeded in staining long, wavy, peritrichous flagella about the bacilli upon specimens of Shiga's, Flexner's, and Kruse's organisms. The proof of the existence of flagella indicated the occurrence of motility under suitable circumstances, and the determination of favorable conditions has now been accomplished.

The method of developing motility is applicable to cultures recently isolated or those cultivated indefinitely outside the body. In the former case a guinea-pig is inoculated intraperitoneally with a dose of the culture that will cause death in 24-36 hours. From the peritoneal exudate a transplantation is made into acid bouillon[2] which is incubated

[1]The publication of Martini and Lentz (*Zeitschr. f. Hygiene u. Infectionskr.*, 1902, XLI, 540) appeared later than this work, but as they are so dogmatic in their statement, especial reference is made to their negative statement.

[2]Acid bouillon prepared from finely cut, lean beef, in the proportion of 500 grms. to the litre of distilled water. After standing 24 hours in the ice-box, the

over night. The bacilli are non-motile. If now transplantations are made successively, from time to time, into test tubes of the acid bouillon, as quickly as the tubes become cloudy from growth, motion will be discovered within from 24 to 36 hours. The successive transplantations may be required every one-half to one hour during fourteen to sixteen hours, a long working day, in order to bring about visible motion in the organism.

In some instances even better results were obtained by diluting the acid bouillon with sterile distilled water in the proportion of 5-10 drops of the former to 10 c.c. of the latter.

This method is somewhat laborious, but it is the only one with which we have succeeded invariably. When applied to older stock cultures it must be further elaborated. The agar-agar cultures used for inoculation must be given in such quantity as to cause the death of a guinea-pig in from 24 to 48 hours. From the peritoneal exudate a tube of acid bouillon is inoculated; from this culture, incubated for 24 hours, a second animal is inoculated and from the acid bouillon culture obtained from this guinea-pig a third one is inoculated. From this third tube, incubated for 24 hours, successive subcultures are prepared and examined at frequent intervals as already stated.[1]

The motion of the bacilli is unmistakable, although not all in a given field are motile. The motion is a tumbling one which carries the moving bacilli into the depth of the fluid and up and down across the field of the microscope. It is easily distinguished from even the most active Brownian movements.

Significance of the Results. The studies presented in this paper leave little doubt of the causal relation of *B. dysenteriæ* to the summer intestinal diseases of children in the cases studied. The proof of this relationship which we have brought forward in this paper, is equivalent to that regarded as sufficient to prove an association of cause and effect between the same bacillus and adult dysentery. The conclusion that the bacillus of dysentery is an important, if not the most important, cause of the summer diarrheas of children seems, therefore, justifiable. In how far the presence of the bacillus may account for the general diarrheal diseases among children, both in the summer and winter, a

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fluid is expressed, 3 grm. sodium chloride and 10 grm. peptone are added, and the whole is boiled, filtered, and tubed. The reaction should be decidedly acid, and the bacillus of dysentery should grow abundantly in 24 hours producing a heavily clouded suspension.

[1]Our thanks are due to Professor Welch for drawing our attention to the use of acid bouillon for demonstrating motility.

larger study, embracing a wide range of cases of intestinal disturbances and distributed over a wide area, alone can determine.

The differences between the pathological changes seen in adult bacillary dysentery and those in the summer diarrhea of infants, as well as the variations met with in the latter disease itself, might well lead one to question the fact that one organism is capable of producing such diverse lesions. But our present knowledge of the varying effects of pathogenic organisms upon the animal body is such as to weaken arguments based upon such theoretical objections.

As yet, it would be premature to conclude from our studies that all cases of summer diarrhea are caused by the *B. dysenteriae.* There are needed studies of additional cases of summer diarrhea and also winter diarrhea of children with the view of discovering the presence of the dysentery bacillus and also the occurrence of the agglutination reaction.

CLINICAL SUMMARY OF CASES OF SUMMER DIARRHEA STUDIED AT THE THOMAS WILSON SANITARIUM, BALTIMORE, DURING SUMMER OF 1902.

BY J. H. MASON KNOX, JR., PH.D., M.D.,

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The results of the bacteriological study carried out by Messrs. Duval and Bassett, as given in the preceding paper, make a brief description of the clinical course of the cases highly desirable. Ten cases are included in the summary in which, although the specific organism was not isolated, the blood of the patients in high dilution agglutinated the dysentery bacilli.

The ages of the patients ranged from three weeks to four years:

From 3 weeks to 6 months	15 cases
" 6 months to 12 months	22 "
" 12 months to 18 months	9 "
" 18 months to 24 months	5 "
Above 24 months	1 case
	52 cases

Of the 52 cases, thirty-six occurred in children under one year, and forty-five of the patients were not older than eighteen months. Of the whole number the only case recorded over two years old was that of a child four years of age who presented symptoms more like those of adult dysentery.

An effort was made in each instance to learn the character of the food and water taken before the onset of the illness.

The raw milk used was usually bought from small grocery stores near by. Of the 33 cases in which positive information as to water could be obtained, it was found in 30 that the water supplied to the baby was unboiled. Sometimes this unboiled water was used as a diluent of the food, but often it was given between feedings. (In but 3 infants it is stated that only boiled water was used both with and between the feedings.) In the 7 cases in which the attacks occurred in breast fed babies, all received unboiled water between their

feedings. Of the 8 infants fed on boiled or sterilized milk, only two were given boiled water exclusively. Other errors are perhaps noteworthy, as in the case of children of one year old or younger who were fed regularly at the family table.

It is difficult to speak from personal experience about the manner of onset, because some days elapsed between the beginning of the symptoms and the admission to the sanitarium. In the majority of cases seen in the first week of illness, the attack in which the child was admitted was usually its first sickness, the history being that the patient, after a day or two of languor, was suddenly seized with diarrhea, succeeded or accompanied by vomiting and sometimes by abdominal pain. Generally there was a rise in temperature with considerable constitutional disturbance. Although most of the patients admitted had already passed this stage, the history of an acute onset was usually

Previous Diet.	Cases.	Water.		
		Boiled.	Unboiled.	Not Stated.
Breast fed	7	.....	7	.....
Breast fed plus condensed milk	2	.....	.....	2
Cow's milk boiled or Pasteurized	11	2	6	3
Raw cow's milk, whole or diluted	16	.....	13	3
Raw cow's milk plus condensed milk	1	.....	1	.....
Condensed or malted milk	13	1	3	9
Total	50	3	30	17

definite. After the acute symptoms subsided, the patient under favorable conditions and proper treatment, went on to convalescence in from a few days to three weeks; but if the infection was more virulent or the resistance of the patient low, there was progressive loss of weight, continued fever, and evidence of inflammatory products in the dejecta. Of the severer grades of infection there were many examples in our series. The temperature range was as a rule not very high, varying usually between 97° and 102° F. It was usually irregular and higher the more acute the illness. Fatal cases often showed a considerable rise ante-mortem.

Vomiting accompanied the diarrhea at the onset in 15 cases in our series. During the course of the illness no history of vomiting was obtained in 13 cases, while in 29 it was described as moderate, and in 10 as excessive.

A brief description of the stools is entirely inadequate to picture the variety in appearance and consistency exhibited by the dejecta. Nearly all of the stools were semi-fluid and consisted in part at least of mucus. They varied in number from 1 to 30 in twenty-four hours and were of all possible shades of color from yellow to grass green; some consisted mostly of fecal matter while others were entirely without it.

The presence of blood in the stools was carefully noted. In a series of forty-eight cases this symptom was especially observed:

No blood throughout the course of the disease in.....	13 cases
Occasional fleck or tinge of blood.....	18 "
Blood moderate in amount, but inconstant.....	10 "
Blood considerable and fairly constant.....	6 "
Stool composed largely of blood.....	1 case
Total.....	48 cases

When blood makes its first appearance late in the disease and is associated with pus, it indicates the existence of an inflammatory process and is of unfavorable significance. In many of the cases in which a considerable amount of blood was present, pus was also apparent to the naked eye and leucocytes were found on microscopical examination.

The length of time the patients remained in the sanitarium averaged about two weeks.

Treatment.—Usually an initial purge of castor oil or calomel was administered. Milk was always stopped entirely in the acute stage and resumed gradually only as the symptoms subsided. In its stead thin cereal gruels with or without egg albumen were substituted, often mixed with broth. Whey was used in many instances and found to be well borne and a convenient step in the return to a milk diet. Gastric lavage was employed for excessive vomiting. The colon was irrigated in selected cases once or twice a day, either with salt solution or a mild astringent solution. Where there had been great loss of fluid because of the frequency of the stools, and symptoms of toxemia were present, hypodermic saline infusions were employed. In general drugs were used sparingly and only for particular symptoms. The following table shows the result in 49 cases:

Discharged cured	20
" improved	14
" unimproved	6
Died	9
	49

Because of the great difficulty in obtaining a reliable clinical basis of classification, any attempt at a grouping of the summer diarrheas must be regarded as tentative. From a study of the histories of these fifty-two cases of infection with the same microörganism, we may divide them into two groups.

I. Acute Gastro-intestinal Infections (dyspeptic diarrhea) of which there were 18 examples. This group showed little or no evidence of being associated with destructive intestinal lesions.

II. Ileo-colitis (dysentery or inflammatory diarrhea) of which there were 34 examples. In this group often the early stages of the disease were similar to Group I; but the greater prostration, the longer duration, the character of the stools, and at times the fatal termination indicated the presence of inflammatory processes in the intestines.

It is well known that the victims of summer diarrhea are chiefly the weak and badly nourished children of the poor, who possess but little resistance. The disease may be a terminal infection, often a mild one, which ends a protracted period of malnutrition. This was the history of 11 of our cases in which the intestinal disease succeeded a long period of wasting. Of these 11 cases, 4 properly belong to Group I. and 7 to Group II. In two cases acute nephritis complicated the intestinal infection and was the direct cause of death. In one case the diarrhea was concurrent with an attack of lobar pneumonia.

But little can be said of the pathological changes from personal experience, as only three of the fatal cases came to autopsy. One belonged to Group I. and two to Group II. The following is a brief summary of the findings in these cases; the state of the gastro-intestinal tract only being given in detail:

Case I.—Stomach: mucosa pale and smooth. Small intestine: no distension; mucosa pale, Peyer's patches moderately swollen; no especial injection of the vessels and no ulceration. Large intestine: the general condition of the mucosa resembled that of the small intestine, but one or two of the enlarged lymphatic nodules showed a minute superficial loss of substance. The mesenteric glands were enlarged, the swelling being noticeable chiefly in the glands of the lower colon and rectum.

This case was complicated with nephritis. The urine during life contained albumin, pus cells and numerous casts. The kidneys were large, pale, and cloudy. Patches of consolidation existed in the dependent parts of the lungs.

Case II.—The stomach and duodenum appeared to be normal. The ileum showed throughout its length small hemorrhages, but no ulceration was detected. The jejunum in its upper third presented a similar appearance to that of the ileum, but the pathological process lessened and disappeared higher up in the intestine. The patches of Peyer were swollen but not ulcerated. The entire colon was dilated; its mucous membrane was thickened and the surface covered with

bloody mucus. In the mucosa were scattered hemorrhages and losses of substance, varying from a pin's head to a split pea in size, the edges being irregular and infiltrated with blood. The meso-colic glands were markedly swollen and the general mesenteric glands were congested and somewhat enlarged. The left lung showed scattered areas of consolidation.

Case III.—The small intestine was thin and pale and showed no focal changes except a few small areas of congestion in the lower ileum. The mucosa of the descending colon was thickened and hyperemic, its surface irregularly pitted but not showing definite ulceration. On the other hand, the mucosa of the transverse colon, cecum and ascending colon showed groups of small ulcers apparently affecting the solitary nodules. All the mesenteric glands were swollen and reddened. The base of the left lung contained a consolidated area.

The pathological conditions above noted while differing somewhat among themselves, differ essentially from the lesions found in adults, and even in children, in the acute dysenteries from which hitherto B. dysenteriae (Shiga) has been obtained. Although the lesions in the intestine in the three cases given present differences, they are not such as to entirely preclude their reconciliation with one pathological process of which they are merely expressions of degree, duration, etc. In view of the fact that in all the B. dysenteriae was found, the question arises whether the essential identity of the lesions may not well be considered, and a revision of the nomenclature of summer diarrhea be attempted upon an etiological basis, the beginning of which through the work of Duval and Bassett we have now secured.

There are many questions bearing upon the pathology of the infantile intestinal diseases that with the advance made may now be regarded as open to solution. Among the most important is the habitat in nature of the Shiga bacillus, the modes of its entrance into the body, the possible rôle played by insects, especially by flies, in its dissemination and the influence of predisposing factors, such as poor and improper food, the manifold improprieties in the care of infants, the effects of high temperatures, as in the warm summer months, and other possible contributory causes to infection which may well be as important as the mere presence of the infecting organism itself.

INVESTIGATIONS DURING THE SUMMER OF 1903.

INTRODUCTION.

BY SIMON FLEXNER, M.D.

At the beginning of the summer of 1903 the Rockefeller Institute for Medical Research undertook, under my direction, the bacteriological investigation of children affected with various forms of diarrhea. The investigation was carried out directly by some 12 bacteriologists in the cities of New York, Philadelphia, Boston and Baltimore. The conditions under which it was conducted were briefly these:

During the previous summer the Rockefeller Institute made a grant of money to Dr. J. H. M. Knox, Jr., of the Wilson Sanitarium for Children, for the purpose of promoting the bacteriological study of infants suffering with so-called "summer diarrhea." This study was carried out by Messrs. C. W. Duval and V. H. Bassett who discovered, in the course of it, in the dejecta and intestines of a high percentage of the children, a bacillus agreeing in essential properties with B. dysenteriae, Shiga. This bacillus was moreover found to undergo agglutination with the diluted blood-serum of sick infants and to be unacted upon, in this respect, by the blood of healthy children or of children suffering from some other diseases. On the basis of this finding of the dysentery bacillus in more than forty ill children, of the total failure to obtain it in the stools of normal children, and of the serum reaction, they felt themselves justified in pronouncing the microörganism the probable cause of the diarrhea from which the children yielding it were suffering.

A year earlier—the summer of 1901—Vedder and Duval investigated several outbreaks of dysentery in adults in this country and found the dysentery bacillus in two institutional epidemics and a number of sporadic cases of the disease. My previous studies upon tropical dysentery, made in 1900, had led me to experiment with the production of a vaccine of the dysentery bacillus which experiments were

later continued under my direction by Dr. F. P. Gay in the Pathological Laboratory of the University of Pennsylvania. The finding by Vedder and Duval of that organism in this country led Dr. Gay and myself to begin the immunization of horses for the purpose of producing a serum[1] which might possibly possess curative power over the bacterial dysenteric diseases of the tropics and the United States. The discovery of Duval and Bassett, which was soon confirmed by Wollstein, gave at once a far wider field of usefulness for this hypothetical curative serum.

The Rockefeller Institute undertook to support an investigation of the bacteriology of the "summer diarrheas" of children and to defray the expenses of testing, as far as might be, upon sick infants the anti-dysenteric serum made from the horse by the injection first of the dead cultures (vaccine) and later of living cultures of B. dysenteriae.

The plan of the investigation which was adopted consisted in the study of sick children in several Eastern cities—Boston, New York, Philadelphia and Baltimore. It was hoped in this way to secure data of value in regard first, to the question of the local or general occurrence of the dysentery bacillus, and next, to the usefulness of the anti-dysenteric serum and to its action upon a considerable number of the patients. I shall deal with the question of the bacteriology of the cases especially, leaving for others the task of reporting the effects of the serum on children.

As the cause of certain, at least, of the diarrheas was assumed to be B. dysenteriae, a concrete problem was immediately presented for investigation. In order that this investigation should have the value of a consistent and moderately uniform undertaking it was necessary that the persons conducting the bacteriological portion of the work should be familiar with the study of the bacterial flora of the dejecta and the method of isolating B. dysenteriae, as well as the manner of carrying out the agglutination tests.

I was fortunate enough to secure as aids upon whom the work of investigation would directly fall several bacteriologists who had already established their ability in this line of study. The remainder of the assistants, while they had not worked so directly with the problem before them, yet had the advantages of a thorough training in the general subject of bacteriology and its methods. To provide, at the outset, for uniformity of method of work I arranged a brief course

[1]Shiga had already pronounced favorably upon a curative serum from Japan.

of instruction at the Pathological Laboratory of the University of Pennsylvania in which the study of the bacillus of dysentery could be pursued. This course was attended, in the early part of June, by a number of those who later took part in the investigation, and by several physicians and advanced medical students who conducted studies independently of the Institute in Washington, Philadelphia and Albany.

The Rockefeller Institute secured the hearty coöperation of numerous hospitals and dispensaries from which the materials for study were drawn, and of several established bacteriological laboratories in which the examinations could be conducted. I shall enumerate the chief sources of the materials and places of study:

Boston: Floating Hospital for Children; Bacteriological Laboratory of the Board of Health. Especial thanks and acknowledgments for many acts of courtesy are due Dr. Hastings and the visiting staff and assistants of the Floating Hospital, and Drs. Durgin and Hill of the Health Department.

New York: Vanderbilt Clinic, Roosevelt Hospital, Babies Hospital, Foundling Hospital, Department of Health, Bellevue Hospital, Post-Graduate Hospital, Nursery and Child's Hospital, Woman's Infirmary and Sloane Maternity. It will, I regret to say be impossible on account of the lack of space to thank adequately the large number of persons who promoted the investigations in New York. But especial acknowledgments are due the New York Health Department and Drs. Biggs and Park in particular, Drs. La Fétra and Howland of the Vanderbilt Clinic, Dr. Prudden, Dr. Holt, Dr. Freeman and the management of the hospitals and dispensaries that so kindly supplied materials or gave the use of laboratories for this investigation.

Philadelphia: Children's Hospital, University Hospital, Pathological Laboratory of the University of Pennsylvania. Thanks are also extended to the medical staff of the hospitals and to Dr. Newmayer of the Jewish Charity Dispensary.

Baltimore: Wilson Sanitarium, Johns Hopkins Hospital and Pathological Laboratory of the Johns Hopkins University. Acknowledgments for courtesies and privileges are due the management of the Wilson Sanitarium, and to Professor Welch and the staff of the Children's Dispensary of the Johns Hopkins Hospital.

The following is a statement of the laboratory organizations:

Boston: Mr. A. I. Kendall, assisted toward the end of the season by Mr. P. A. Lewis.

New York: College of Physicians and Surgeons: Dr. C. W. Duval assisted by Mr. E. H. Shorer. Babies' Hospital: Dr. Martha Wollstein, assisted by Dr. Grace Dewey. University and Bellevue Hospital Medical College: Dr. F. P. Gay, assisted by Dr. E. McD. Stanton. Woman's Infirmary: Dr. Louise Cordes.

Philadelphia: University of Pennsylvania: Mr. P A. Lewis (until transferred to Boston).

Baltimore: Wilson Sanitarium: Dr. V H. Bassett, John Hopkins University: Mr. W. W. Waite, associated for a brief period with Mr. E. H. Shorer.

The separate reports which follow, in which the results of each laboratory are given, contain brief descriptions of the methods of work; but it will, perhaps, be desirable to state in this place some of the general facts relating to the subject of investigation.

Since the demonstration by Pfeiffer of bacteriolysis and the application of the phenomenon to the diagnosis of typhoid fever by Widal, agglutination of bacteria by diluted blood-serum has been much employed in the diagnosis of bacterial diseases. Although closer and more searching study has exposed certain fallacies to which the test is subject, yet the latter have served to establish more definitely the limits of its application. And hence the general statement, to which the exceptions are relatively unimportant, can still be made, to wit: agglutination of bacteria by well-diluted blood-serum is an indication of infection with the bacteria agglutinated.

The value of this general fact becomes enhanced if it is shown that under conditions of ordinary health, and in the course of certain forms of disease, this agglutinative reaction is absent; while at the same time it appears regularly, or at least with great frequency, when a definite kind of pathological state of the body exists.

This form of reasoning, which led Shiga some five years ago to a renewed study of the acute dysentery of Japan with the result, as is now widely known, of discovering the bacillus which bears his name, led me a year later (1900) to a similar investigation of tropical dysentery in Manila with a result agreeing in all essential respects with that of Shiga. Since this time and through the use of the same methods the cause of the dysentery of other countries, in temperate and tropical climates, has been discovered to be identical with, or closely allied to, Shiga's bacillus. The application of the method to the study of a group of cases of infantile summer diarrhea by Duval and Bassett gave, as has already been stated, similar results.

It is unfortunate for the nomenclature of bacillary dysentery that

doubts and disagreements regarding the nature of certain strains of dysentery bacilli should have entered into the discussion of the cause of the disease. And it is even more unfortunate that local zeal should have been permitted to usurp the place of scientific accuracy in establishing the priority of discovery and the precise nature of the bacillus of dysentery.

As the type of the bacillus must be taken the organism described by Shiga in 1898 and 1899. With this type the bacillus isolated by Kruse in 1901 is in such close agreement as to be indistinguishable even by the most refined tests, and hence for this latter organism there can be claimed no independent position. Kruse's observation has the value of establishing the application of Shiga's discovery to a class of cases of dysentery occurring in Germany.

At the time of my investigation of tropical dysentery I identified the bacillus which I isolated as Shiga's bacillus. Since that period, and indeed within a short time, differences in action of the two bacilli upon certain fermentable substances, and in degree of agglutination with serum derived from immunized animals have been described, so that at present the two organisms are looked upon as representing distinct types of dysentery bacilli. When it is recalled that the early tests of agglutination were made with human serum, and that the action of the bacilli on the sugars had been little studied, and, further, that in colony-form and usual cultural properties no differences are to be seen, it becomes evident why the bacilli should have been classed as identical.

Kruse was the first to point out a marked variation in degree of agglutination between different strains of dysentery bacilli. The two sets of cultures which he studied came respectively from an epidemic of dysentery occurring at Laar and several cases of the disease which arose in an institution for the insane. On the basis of the observed difference he proceeded to designate the former as the "true" and the latter as the "pseudo-" dysentery bacilli.

Even should the fact of the essential difference of the organisms be admitted the appellations are most unfortunately chosen. Admitting for a moment, as Kruse would have it, that the second type of bacillus is the cause of asylum dysentery, it assuredly does not set up a condition that can properly be termed "pseudo-dysentery"; and if not this, then the bacillus should not be called "pseudo-dysentery" bacillus. There has been brought forward no evidence upon which one of the pathological processes may be assumed to be dysenteric rather than the other, for the anatomical lesions are in essential agree-

ment, and mere chronology of investigation can hardly be taken as distinguishing the "true" from the "false" organism. Time has considerably cleared up the distinctions noted by Kruse and has upheld his view of the variation in agglutination, and it has also shown us, important physiological differences between the two types. But while this support has been forthcoming time has shown his view of the distinct origin of epidemic and asylum dysentery to be erroneous. This last contention has been disproven especially by the studies of Vedder and Duval of two epidemics of dysentery occurring in almshouses and insane asylums at New Haven, Conn., and Lancaster, Pa. They found in certain of the cases the "Shiga" or "Kruse" *true* dysentery bacillus, and in others the type of bacillus first obtained by Flexner* in the Philippines with which the "pseudo-dysentery" bacillus of Kruse has been found to agree.

Lentz has recently prepared a differential culture medium which has seemed to distinguish readily and accurately the two types of dysentery bacilli. By using a medium containing mannite he found that certain strains of the bacilli did not act upon it while others attacked it with the production of acid. Among the cultures tested by him were those of the following origin: Shiga (Japan), Kruse (Germany), Duval (New Haven), and Müller (Styria), all of which left the mannite unaffected, and Flexner (Harris, Manila), Strong (Manila), and Kruse (pseudo-dysentery) which attacked that substance energetically. These results have been controlled by Martini (and himself) with the serum of a goat which had been immunized by means of a culture of the first or "Shiga" type of the bacillus of dysentery the agglutination value of which for that type was 1:600 and for the second or "Flexner-Harris" type 1:25 to 1:50. Hiss and Russell confirmed the studies of Lentz and introduced a valuable additional differential culture-fluid—their serum-water medium.

The foregoing data upon the types of dysentery bacilli lead us to conclude that the fact of their general cultural agreement is overshadowed by the differences displayed by them in their action on mannite and response to a single kind of artificial agglutinative serum. And yet evidence is not wanting to show that in agglutination-value the two types are not wholly distinct, for which we can adduce the fact of the action upon both types of bacilli of human serum in cases of dysentery and "summer" diarrhea.

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*The special strain of this bacillus which has been extensively studied came from a soldier named "Harris"; hence the designation "Flexner-Harris."

While normal human serum in considerable concentration is without agglutinative effect upon the bacilli, the serum of dysenterics agglutinates both types of bacilli and often in approximately the same degree. The dysentery bacilli isolated in 1902 by Duval and Bassett from children have since been shown by the studies of Gay and Duval to consist exclusively of the "Flexner-Harris" type; and yet Duval and Bassett found that the blood-serum of these children acted upon both types of bacilli in respect to agglutination. Since the "Shiga" type of the organism is supposed to agglutinate less readily than the "Flexner-Harris" type (to be less susceptible to chance agglutinins according to Kruse and Martini and Lenz), the occurrence of active agglutinins in these children for the "Shiga" bacillus speaks unmistakably for the ready development in human beings, of agglutinins for both of the types of bacilli as a result of infection with a single type.

The serum of the horse would seem to contain normally at times agglutinins for a considerable number of bacterial species. Bergez has recently studied these normal agglutinins with especial reference to certain water bacteria. For this purpose he employed anti-dysenteric serum of the horse (supplied by me) and he found that the removal from the serum of the agglutinins for those bacteria left the specific agglutinins for dysentery bacilli practically intact. Gay has also made out that in spite of the occurrence of natural agglutinins in horse serum for B. dysenteriae, the artificial immunizing with cultures of the bacillus increases the agglutination-value of the serum so immensely as to render inconsiderable and hence negligible for cross testing, the normal agglutinins. He ascertained the fact that as the agglutinins for one type of the bacillus are raised by immunization that the agglutination-value of the serum for the other type rises; and hence the proportion is not a fixed one for the two types of the bacilli, since one does not remain stationary while the other rises, but that this proportion is capable of variation at will within the limits of artificial immunization and corresponding agglutinin production. Using horses' serum of relatively high agglutination-value Gay obtained figures and proportions of cross agglutinations which showed those of Martini and Lentz, who employed a weak artificial goat's serum, to be much too low. Thus the serum of "Shiga" horses gave the proportion of 6:1 to 30:1 as regards the "Flexner-Harris" type, and of "Flexner-Harris" horses the proportion of 5:1 to 10:1 as regards the "Shiga" type.

The question of the relationship of the types of dysentery bacilli is so important that I shall discuss briefly another aspect of the subject.

Dysentery bacilli are subject to bacteriolysis *in vitro* either by means of fresh normal or fresh immune horses' serum. For the purpose of studying the comparative bacteriolysis of the two types of bacilli both serums are employed.

Shiga first applied the method devised by Neisser and Wechsberg to the bacteriolysis of dysentery bacilli, but his study had no reference to the differentiation of the types. A word upon the method may be in place: A fixed quantity of normal fresh horse's serum, incapable in itself of producing bacteriolysis, will, in the presence of a definite amount of inactivated immune-serum, cause complete destruction of a given weight of dysentery (or other) bacilli. The addition of more or less immune-serum than is exactly required will allow of greater or less growth of the organisms, according as a deficiency or an excess of amboceptors is present in the mixture. An insufficiency of immune-serum prevents complete bacteriolysis by failing to supply all the amboceptors needed to unite the complements to the bacteria; an excess of immune-serum also prevents complete bacteriolysis by introducing so large a number of amboceptors as to bring about their union directly with the complement (without any attachment to the bodies of the bacteria) and hence its deviation from the bacteria.* Since it is the complement that destroys the bacteria, should it become deviated from the bacteria, then no destruction takes place.

Gay, while working under a grant from the Rockefeller Institute, in my laboratory at the University of Pennsylvania, found that the bacteriolysis of dysentery bacilli as observed under these conditions, was dependent upon the employment of bacilli and immune serum of corresponding types. Neither immune serums nor types of bacilli were mutually interchangeable in producing bacteriolysis, from which fact the conclusion that bacteriolytic variations serve to distinguish the two types of bacilli could be drawn.

From the facts enumerated it will be evident that the more recent studies upon Bacillus dysenteriae have tended to establish more and more firmly the belief in the existence of "types" of the organism. Between these types the similarities are perhaps no more important than the differences; but no facts have thus far been brought forward which would indicate that one rather than the other acts pathogenetically upon human beings. This last consideration is of commanding importance in respect to the possible employment of an artificial immune serum in combating infections with the bacilli in man.

*It is needless to point out that the explanation of the facts of bacteriolysis under the conditions named is hypothetical.

Since the finer reactions tend to separate the two types of bacilli the question which presses for solution is whether the action of protective immune serum is as distinct as the mannite, agglutination and bacteriolytic reactions. Upon the answer given to this question may depend the practicability of using therapeutically anti-dysenteric serum.

Shiga's immune serum is polyvalent and prepared by injecting several strains of dysentery bacilli into the horse. Whether or not all the strains employed represent the "Shiga" type of bacillus is not known; for the differentiation now recognized was undiscovered when his serum was first made. Indeed, it is not stated whether more than one type of the bacillus occurs in Japan. Hence his serum is not adapted either to the study of bacteriolysis in the manner introduced by Gay or to the testing of a cross process of immunization such as is now to be described.

At my request Dr. Gay made a careful and exact study of cross-immunization of guinea-pigs with the "Shiga" and "Flexner-Harris" types of bacilli and immune serums. Fortunately an unlimited quantity of serum was available as we had had several horses in process of immunization with the different types during a period of two years.*

As the dysentery bacillus tends to diminish in virulence when cultivated outside the body it is necessary that a standard of activity be established and maintained by frequent passage of cultures through guinea-pigs. By choosing animals of a fixed weight and the injection of a determined quantity of active culture, death takes place regularly in from 18 to 24 hours. The suspensions of the bacilli were injected intraperitoneally, and when immune serum was employed it was introduced beneath the skin.

The experiments on cross-immunization and infection proved to be very important in that they showed that the protective power of the serum is a factor which fails to proceed hand in hand with bacterioly-

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*It is proper in this place to acknowledge our indebtedness to the Rockefeller Institute for Medical Research which promoted by money grants the study of immunization, and to the H. K. Mulford Company of Philadelphia which generously provided the large number of horses used in the course of this study and the subsequent tests of the immune serum upon children. The H. K. Mulford Company also rendered us invaluable aid through their laboratory staff, and we wish to thank the gentlemen composing it, and especially Drs. Kinyoun and Lincoln, for their many courtesies and the ready and very able help which they rendered us. It was a great convenience later on, while conducting the tests upon children suffering from diarrhea, to have the immune serum provided us in sterile glass syringes for immediate use, which the H. K. Mulford Company supplied without cost.

sis by serum, and that the latter phenomenon is not a measure of the possible usefulness of the serum as a therapeutic agent. On the other hand, the experiments also proved that the protective power of the serum is greater for an organism of a corresponding than for a so-called "crossed" type. Stated in actual figures almost twice the quantity of serum is needed to give for the "crossed" a protection equal to that given for the same type of bacillus.

At the beginning of the summer of 1903 Bacillus dysenteriae, first found by Shiga in Japan in 1898-99, had been proven to be intimately associated, and probably the cause of acute endemic, epidemic, sporadic and institutional dysentery over practically all the world. The organism had further, through the studies of Duval and Bassett, been shown to bear a similar intimate relationship with a certain class of cases of diarrhea arising in children during the warm summer months and by Wollstein to such cases occurring in the winter. A closer study of the bacillus, had led to its separation into two groups according to certain distinctive reactions. Shiga had already produced a polyvalent immune serum with which he had successfully treated the acute dysentery of Japan, and Flexner and Gay had completed the preparation of a series of monovalent immune serums which they proposed to have used in the treatment of bacillary dysentery in Manila and the United States, and of children suffering from infection with the bacillus of dysentery. Gay had shown that an effective protection by mean of immune serum is possible without reference being paid to the special type of bacillus causing the infection or employed to produce the anti-dysenteric serum.

In the summer of 1903, as has been stated, I was enabled through a liberal grant of money from the Rockefeller Institute for Medical Research and the co-operation of a group of skilled bacteriologists to direct an investigation of the bacteriology of diarrheal diseases occurring in a large number of children, and to have tested upon a number of these children, suffering from infection with Bacillus dysenteriae, an anti-dysenteric serum prepared from the horse.

The separate reports which follow upon the bacteriology of the cases containing the results arrived at by the different workers have been edited by me. The results are, however, entirely the property of the workers, as my share in the investigation consisted in the exercise merely of a general supervision and control which in no vital way affected the individual work of the investigation.

A separate and distinct report upon the results of the injection into

children of the anti-dysenteric serum will be included in this publication.

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REPORT OF C. W. DUVAL, M.D., ASSISTED BY E. H. SHORER, STUD. MED.

The study, the results of which are to be given in this report, was carried out in the bacteriological laboratory of the College of Physicians and Surgeons, New York, which was placed at our disposal through the kindness of Professor Prudden. We cannot be too grateful to him and to the staff of the laboratory for the courtesies which were shown us and the thorough manner in which our work was facilitated. Without this cordial help and cooperation the results of our work must have been less satisfactory and complete than we were able, through this assistance, to make them.

The entire number of sick infants, studied during the months of June, July, August and September, was 79. The study actually began on June 15th, and closed about the end of September, continuing, therefore, three and a half months. The materials of the study, which consisted of dejecta, were chiefly drawn from the Vanderbilt clinic. Roosevelt and Post-Graduate Hospitals furnished six cases, and a few were private patients (see table). From these cases we obtained the bacillus dysenteriae (Shiga) in greater or less numbers from 75, or in 94 per cent., of all the cases examined. The clinical symptoms and course of the disease were so varied as to include all grades of cases, from the mildest to very severe forms of diarrheal disease. And in keeping with this fact the stools which came to us for examination varied within very wide limits, on the one hand consisting almost wholly of feces, and, on the other, of blood and mucus practically without fecal contamination.

Isolation of Bacillus Dysenteriae.—The character of the dejecta with which we worked, as compared with that studied by Duval and Bassett, led us to modify the technique recommended by the latter in their publication. Since Duval and Bassett dealt especially with stools containing mucus and blood and had their chief success with that type of stool, and as the material furnished us contained many specimens from which mucus and blood in more than notable quantities were absent, we found that a more rigid examination than previously made would be required either to exclude with toler-

able certainty the finding of the bacillus, or to demonstrate it among the large number of bacteria with which it was often associated in cultures.

We found the use of fresh-stool specimens of the utmost importance, *i.e.,* specimens obtained immediately after passage. While stools rich in the bacilli may be dealt with successfully after a longer interval of time, or may be made to yield the dysentery organism with less trouble than the process we are to describe involves, success with many specimens can, we think, be obtained only by the exercise of laborious care. The procedure which we pursued is as follows:

Mucus is to be selected for the plating, and when this is attached or adjacent to fecal matter it is to be teased away from the latter by means of a stiff, sterile platinum loop. The mucus is now suspended in normal saline solution or bouillon, the mixture well shaken and set aside for a few minutes in order to permit the washed mucous flakes to settle. The upper two-thirds of the fluid becomes clear of visible particles, but presents a cloudy appearance, due chiefly to the suspended bacteria. From this cloudy fluid are prepared twelve (12) Petri plates in neutral agar-agar, using one to two loopfuls of the suspension for each plate. The decision whether to employ one or two loops for the plating will depend upon the degree of cloudiness which is brought about by the number of suspended bacteria.

By proceeding in this way and plating from two separate suspensions of mucus we obtained about 25 plates, which, as a rule, is the smallest number with which we worked. The seeding of these plates should be regulated so that the total number of colonies developing on a plate shall number between 50 and 100. By paying attention to the degree of cloudiness of the fluid and adjusting to this the number of loops carried in to the agar-agar it is easily accomplished. We have found this method preferable to the use of a stronger initial suspension of bacteria and the employment of a second and third dilution as is generally practiced.

In incubating the plates are inverted and left in the thermostat at 37° C. from 14 to 18 hours. At the end of this period every small *pearl gray* colony is transplanted to Hiss' semi-solid medium. All colonies are now marked on the glass with a wax pencil and the plates kept inverted at room temperature for one week at least, observations upon the development of new colonies being made daily. We may remark here that in order to avoid the rapid desiccation of the agar-agar the plates are not returned to the thermostat. As it is of advantage to have the medium form a thin layer in the plate so that surface col-

onies chiefly develop, drying is to be avoided as much as possible. All new colonies which appear are sub-cultured into the semi-solid medium. The character of the growth of the dysentery bacillus in this culture material will be described presently but in this place it should be stated that if that bacillus does not appear among the tubes prepared in this way, all the markings are to be erased from the plates and every small colony that resembles in form and color colonies of Bacillus coli communis or Bacillus typhosus is to be transplanted to the semi-solid medium.

The inoculated tubes are ready for examination after having been kept at 37° from 3 to 6 hours. All tubes showing a cloud throughout are discarded for it is brought about by the presence of actively motile bacilli, among which B. dysenteriae is not contained, and all tubes showing gas formation are also excluded. Those tubes which present a slight haziness or show growth along the needle track only are tested for gas production by careful stirring with the platinum needle. Any disengaged gas collects in the form of small bubbles, and all tubes in which these appear are also put to one side. Only such tubes as exhibit no bubbles are examined further.

The next step is to test with anti-dysenteric serum all cultures not forming gas in which the morphology of the organisms is that of colon-typhoid bacilli. For this purpose a small quantity of the growth is suspended in salt solution. We used the serum of the horse supplied by Dr. Flexner for carrying out these tests. All bacilli showing a positive agglutination are sub-cultured into litmus milk and the serum-water medium of Hiss. In some instances we also sub-cultured into media containing other sugar, e.g., dextrose, maltose, saccharose, and also dextrin.

Identification of Bacillus Dysenteriae.—The usual plan which we pursued in our study was to identify the bacillus by cultural tests before applying the serum reaction, for one learned that the immune serum of the horse will sometimes bring about the agglutination of bacilli which do not agree culturally with the dysentery bacillus. We found some such nondescript bacilli which reacted in dilutions of 1 :500 of serum.

The most reliance is to be placed upon the growth of the bacillus in litmus milk observed over a period of several weeks. The true organism produces first acidity, which turns the fluid lilac in color, and after some days this initial acidity gives way and the color returns to that of the control (amphoteric reaction and first alkali production). The next change develops much more slowly and may not become distinctly

visible for several weeks, when the milk will show a more marked alkaline reaction (second alkali production), which is the final change.

Although no stress has been put upon the consideration of the colony form, growth upon agar-agar slants, etc., these features have not been overlooked; but as they are less conclusive than the milk-reaction, agglutination, and the behavior of the bacillus in the special media mentioned, their use is not emphasized in this place.

In the course of our work we paid special attention to the types of dysentery bacilli, which we isolated from dejecta. For the differentiation of the two types—so-called "acid" and "alkaline" types as tested upon the litmus-mannite medium, we soon discarded the use of that material for the mannite-serum-water medium of Hiss. It will be found that the latter is exactly as useful as the former and has the advantage of being easily and much more quickly prepared—a gain not to be considered lightly when hundreds of separate colonies of the bacilli are to be tested. Whereas it requires 48 hours to rid the beef juice of all muscle sugar by means of fermentation (by the use of B. coli com.) in preparing it for conversion into a nutrient medium, the serum is ready at once for use without further treatment. If it is desired to have a solid medium, the litmus-mannite agar-agar can be made from peptone water without any beef or even without beef extract; and although the growth of bacilli may be less vigorous than in the samples containing beef it is sufficient for the purpose of separating the types of the organism.

In carrying out the differentiation of types we carried into the serum-water media (for we employed serum-water containing mannite, dextrose and dextrine respectively), every colony growing upon the semi-solid medium in a characteristic manner, and giving an agglutination result. The interpretation of the action of the bacilli upon these media is important and offers no special difficulty. Since acid production is associated with coagulation of the medium, and both types of bacilli attack dextrose with the formation of acid it follows that all dysentery bacilli bring about coagulation of the serum-water dextrose medium. Since, on the other hand, the "Flexner-Harris" type of organism splits mannite and the "shiga" type does not, the former also brings about coagulation of the serum-water mannite fluid. The use of a special fluid in which dextrin supplants the sugars serves to separate still further the "Flexner-Harris" type of organism into two groups—fermenter and non-fermenter of dextrine, or, according to Hiss and Russell—B. dysenteriae "Harris," from B. dysenteriae "Y."

On the Numerical Relations of Bacillus Dysenteriae.—In many of

our cases the colonies of dysentery bacilli which grew upon the plates were few and not infrequently the bacilli would be obtained from one or two plates only of the series. In other cases the number of colonies was much greater, and in a few instances very large. Since in our experience the character of the stool is no reliable guide to the presence or absence of the bacilli, every stool is to be investigated exhaustively, and a second or third specimen employed before closing the case as negative. We have at times succeeded by such repeated examinations in retrieving what seemed failures at the outset. We have failed to recover the bacillus from a fresh bloody discharge and succeeded at the first attempt with a very unfavorable looking specimen; but as a rule a mixture of blood and mucus or a simple mucus specimen can be regarded as the most favorable material to work with.

We failed in four instances to obtain the dysentery bacillus from cultures. In two of these (dispensary cases) second specimens were not secured; one of those examined was a mixture of blood and mucus, and hence should have been favorable, while the other was twenty-four hours old when received, and therefore unfavorable.

Several of the specimens in our series were of unusual interest and we shall therefore give their histories in some detail:

Case No. 44 yielded a large, semi-solid, green muco-fecal stool in which there was no trace of blood. From the mucus portion 16 plates were prepared. At the end of the first 24 hours (37° C.) the plates showed no colonies of any sort to the naked eye; at the end of the second 24-hour period (37° C.) 9 colonies had appeared. All these proved to be colonies of B. dysenteriae. The plates were now kept at the room temperature for about 10 days and the new colonies transplanted as they appeared. On the fourth day 24 new additional colonies had developed on all the plates; these also proved to be B. dysenteriae. No other colonies appeared and hence the mucus of this specimen is to be regarded as containing the dysentery bacillus in practically pure culture.

Case No. 45 yielded a large, soft, offensive fecal stool containing some mucus but no blood. Twelve plates were made from the mucus. Seventy colonies were transplanted at the first picking, 60 of which proved to be B. dysenteriae. This transplantation took place 18 hours after beginning incubation, and although the plates were kept under observation for 10 days no more colonies of any sort developed. Had the method of "marking" and further incubation been adopted in this case negative results might have been obtained.

Case 71 is to be placed alongside case 44 as respects the predom-

inance of the bacillus of dysentery. Dr. La Fétra prepared the plates at the home of the patient at a distance from the city from the green, blood-flecked mucus of the discharges. Every colony—deep and superficial—which developed on the plates, numbering 70 in all, was transplanted and all proved to be growths of B. dysenteriae.

We wish to place beside this series of cases yielding the dysentery bacillus in very large numbers the following example in which a single colony of the organism was secured with great difficulty from a specimen theoretically favorable to the isolation of the bacillus. Case 46 gave a small, odorless, blood-stained mucous stool devoid of fecal matter. Sixteen plates were prepared and after painstaking search and the transplantation of many colonies a single tube of the "Shiga" type of the bacillus was obtained.

Finally, Case 50, which gave a large but offensive light-yellow, blood-flecked mucus and fecal movement failed to yield from the 18 plates prepared a single colony of B. dysenteriae.

Bacilli Not Certainly Identified as B. Dysenteriae.—In the course of our studies we encountered two bacilli, which may represent still further variations of a common bacillus dysenteriae, or may, perhaps, be entirely independent of that family of organisms. The facts that the variations which we shall point out are physiological and not greater than those which are already admitted in the group, makes it at least probable that the bacillus to be described immediately is a member of the group.

In cases No. 3 and 6 of our series we isolated a bacillus which agreed morphologically, in staining properties and in the usual cultures with a typical control of B. dysenteriae and it agglutinated in considerable dilutions with anti-dysenteric serum. The chief differences noted were its action upon milk and upon lactose-serum-water fluid.

The stool of Case 3 was fecal, but contained some mucus. From the mucus 20 plates were made, and only two colonies of the bacilli to be described were isolated. Besides B. coli communis many streptococci grew upon the plates. The agglutination tests were positive, 1:800 with Shiga A.D.S., and 1:2,000 with Harris A.D.S.*

The bacilli caused first an acidity of the milk which developed properly (*i.e.*, within 48 hours), and next, after a few days, a return to the original hue (alkali production). No further change was noted for 5 to 6 days, when a second acid change, more marked than the first and permanent, took place. The milk did not coagulate even after

*A.D.S.=Anti-dysenteric horse serum.

many weeks of observation. That this bacillus attacks lactose and that the second acidity is brought about by this action is rendered certain by the lactose-serum-water medium which is both acidified and coagulated by the bacillus. As in the case with the true B. dysenteriae it acidifies and coagulates dextrose-serum-water. The two colonies of bacilli from this case which thus far agree in their properties are separated from each other by the employment of dextrin-serum-water which is acidified and coagulated by one and not by the other culture.

From Case 6 a muco-fecal stool was obtained. From the mucus 14 plates were poured; from the plates 10 colonies of a bacillus resembling B. dysenteriae were isolated. The predominating organisms developing upon the plates were B. coli com. and unidentified motile bacteria. The ten colonies mentioned were all obtained from a single plate. They agreed with the bacilli from Case 3 in all respects, and like them were separable into two classes according as they split or failed to split dextrin with the formation of acid.

The ability of this bacillus to act upon lactose with acid—but not with gas—production, is, as would be predicted, constant and unaltered by repeated plating and sub-culturing. It is hoped that its properties may be studied in more detail later.

Bacilli Resembling B. Dysenteriae, but Certainly Identified as Distinct.—We encountered in several instances (Cases No. 11, 13, 22, 28, 38, 46) bacilli which in early cultures may be mistaken for the Shiga type of the dysentery bacillus, although finally they would be distinguished from that organism. In morphology and staining reactions and in cultures upon the ordinary fluid and solid nutrient media it cannot be told from B. dysenteriae. The agglutinations, too, are positive with horses' anti-dysenteric serum, as the bacillus has reacted in dilutions of 1:500 to 1:1000. The media which serve to differentiate the bacillus are litmus milk and the Hiss semi-solid jelly.

In litmus milk it causes the primary acidity, after which there is the return to the original color, but instead of now going on to a mild alkalinity, the milk assumes a deeper blue-black color. The first isola- the lactose-serum-water medium which is both acidified and coagulation), but in distant sub-cultures this property is lost. The semi-solid jelly often brings out a difference more quickly, for a part of the bacilli of this type are sufficiently motile to cloud that medium, which the dysentery bacillus does not do. Another part of the bacilli, however, is more feebly motile, or possibly non-motile, and leaves the semi-solid medium unclouded. With this portion the differentiation is brought about by the litmus milk after a sufficiently long observation.

The serum-water medium is useless for this purpose, as all the sugars except dextrose are unattacked, in which the bacillus agrees with the "Shiga" type of the dysentery bacillus. On the other hand, in the mannite-litmus-agar-agar the growth is indistinguishable for about a week, but after this period a cloud-like spreading away from the line of stab may be noticed by which the separation from similar cultures of B. dysenteriae, which we have never noticed spread, may be made.

We have compared this bacillus with a culture of B. fecalis alkaligenes and found that the latter organism does not act upon dextrose, which the preceding bacillus never fails to do.

Two rabbits were immunized with cultures; their serum agglutinated the bacilli employed for injection in dilutions of 1:20,000. With this serum the "Shiga" and "Flexner-Harris" types of dysentery bacilli reacted in 1:25 dilution for the former and 1:50 for the latter, indicating an absence of cross-reactions with the immune serum of the rabbits.

Case 11. Stool semi-liquid mucus; 12 plates prepared; 7 colonies of B. dysenteriae isolated. The cultures contained both types of bacilli, of which 5 were of the "Flexner-Harris" and 2 of the "Shiga" type. The alkali-producing bacillus was of the motile variety.

Case 13. Stool yellow mucus with flecks of blood; 24 plates made; 30 colonies of B. dysenteriae isolated. Both types of bacilli—2 of "Harris" and 28 of "Shiga"—present. The alkaline bacillus was present. Whether motile or non-motile variety has been overlooked.

Case 22. Semi-liquid green mucous stool; 12 plates poured; 22 colonies of "Flexner-Harris" type of dysentery bacillus isolated. Many colonies of the non-motile variety of alkaline bacillus obtained.

Case 28. Muco-fecal stool; 20 plates made; 7 colonies of "Flexner-Harris" type of B. dysenteriae picked off. Numerous motile, alkali-producing bacilli present.

Case 38. Green, muco-purulent stool; 17 plates made; 6 colonies of B. dysenteriae picked off; 4 "Flexner-Harris," 2 "Shiga" type. The variety of the alkali-forming bacillus overlooked.

Case 46. Small stool of mucus containing blood; 16 plates prepared; this favorable case theoretically yielded, after painstaking search, a single colony of the "Flexner-Harris" dysentery bacillus. Besides this colon bacilli, streptococci, B. proteus and the alkali-producing bacillus (variety not stated) were present.

The above cases briefly stated, in which the alkali-producing bacillus was found, contained at the same time the true dysentery bacillus. A noteworthy fact and one to which we shall return is that in 3 of the

5 cases both types of the latter organism were present. In view of this finding the appreciation of the extraneous alkali-forming bacillus is of great importance.

Single and Double Infection with Bacillus Dysenteriae.—We shall for the present denominate as single infection those cases in which a single type, and as double infection those cases in which the two types distinguished as "Shiga" and "Flexner-Harris" varieties are found. An examination of the table will show at a glance the great preponderance of the "Flexner-Harris" type of bacillus in the cases studied by us, which fact is in keeping with Gay and Duval's studies, in regard to types, of the bacilli isolated by Duval and Bassett in 1902. However, 17 of the cases studied in 1903 showed the "Shiga" type of bacillus. Of these 17 cases the organism was alone present in 11 and associated with the "Harris" organism in 6 instances. Hence, using our small material of 74 positive cases as a basis of conclusions, we can say that single infection with the "Flexner-Harris" type of bacillus is most common, that single infection with the "Shiga" type of bacillus is far less common, and that double infection with both organisms is least common in the diarrheal diseases of children.

Does Any Relation Exist Between the Type of Bacillus and Character of the Dejecta?—Although it is our experience that the character of the stool is no certain indication of the presence of dysentery bacilli in isolatable numbers, yet the stools in which mucus or mucus and blood are present in more than perceptible quantities rarely fail to yield the organism. However, we have failed with a given stool and succeeded with a subsequent one of a like character from the same patient. And while solid or semi-solid fecal material is, as a rule, unpromising, yet in rare instances the dysentery bacillus has been isolated from it.

Since adult dysentery has, so far as is at present known, been associated chiefly with the presence of the "Shiga" type of bacillus, it seemed to us worth while to inquire whether the children in whom that type of bacillus was found presented any peculiarity of infection worthy of notice. Examination of the records of the stools from which the "Shiga" type of bacilli were obtained has revealed the facts that in 6 instances no blood occurred, in four instances it was present as "flecks," and in only one instance in more marked amounts. All the stools, on the other hand, showed mucus, and except in two instances in considerable quantities. With one or two exceptions feces were admixed with the mucus.

The cases in which double infection occurred were not distinguish-

able so far as the stool-condition was concerned from the cases of single infection with the "Shiga" type of bacillus. Blood was rarely present in the stools and never in larger quantity than "flecks," while mucus was abundant. In about half the cases, that is in three instances, fecal matter was quite absent and in two samples pus was visible to the naked eye.

Since the cases which we examined this year were characterized by far less blood in the movements than occurred in the series of cases studied in 1902 by Duval and Bassett, the character of the stools in all the infections may be looked upon as in agreement, by which is meant that the severer cases in which much mucus existed as well as very light infections in which little mucus occurred, arose in the course of all forms of infection, whether single with either type of the bacillus or double with both types of bacilli.

Now that it would appear as if no distinction can be made in the degree of infection as regards the type of infecting organism, the question arises as to whether any relation exists between the severity of the lesions and the number of dysentery bacilli which can be isolated from the stools. This question has already been answered by Duval and Bassett, who regarded cases in which the movements consisted of blood and mucus as most favorable to the finding of B. dysenteriae. An examination of the table given herewith will give our answer to the question, which is that the presence of fecal matter in the movements tends to reduce the number of dysentery bacilli recovered from the plates. But when there is much mucus present and the plating is carried out quickly with the fresh stools, the fecal admixture is of far less importance in affecting the ultimate result. We are therefore led to think that *intra vitam* the mucus is the habitat of the dysentery bacillus and the colon bacillus is inhibited from a free development beside this organism; but outside the body the latter organism may quickly invade the mucus and overgrow or suppress the former bacillus. That putrefactive changes in the intestinal contents affect unfavorably the subsequent isolation of the bacillus of dysentery is indicated by our results with offensive stools (cases 30 and 50).

Concerning Bacillus "Y."—After the description by Hiss and Russell of a variety of dysentery bacillus differing from the "Flexner-Harris" type by virtue of its inability to attack dextrine, we noted the cases in which this variety was present. By referring to the table it will be seen that whereas the "Flexner-Harris" bacillus occurred 55 times, bacillus "Y" occurred 12 times and in all but one instance it was associated with the "Flexner-Harris" bacillus. Its number, as indicated by the

Clinical Case Number.	Plates Made.	Dysentery Colonies Isolated.	Fermenters of Mannit.		Non-fermenters of Mannit. ("Shiga.")	Blood in the Stool.	Mucus in the Stool.	Feces in the Stool	Brief Description of the Stool.
			"Harris."	Bacillus "Y."					
1	24	22	22	0	0	0	+	+	Large mucous stool.
2	24	46	46	0	0	0	+	0	Small mucous stool.
3	20	2	2	0	0	0	+	+	Large muco-fecal.
4	28	47	47	0	0	0	+	0	Small mucous stool.
5	20	1	1	0	0	0	+	+	Yellow fecal stool.
6	14	10	8	2	0	0	+	+	Muco-fecal.
7	13	4	2	0	2	0	+	+	Brown semi-solid.
8	13	8	1	0	7	0	+	0	Yellow mucus.
9	15	1	1	0	0	0	+	+	Yellow mucus.
10	20	39	39	0	0	0	+	+	Yellow muco-fecal.
11	12	7	5	0	2	0	+	+	Muco-fecal.
12	15	20	20	0	0	0	+	+	Semi-liq. mucus.
13	24	30	1	1	28	+	+	+	Green muco-fecal.
14	12	20	20	0	0	+	+	0	Blood-flecked mucus.
15	20	1	0	0	1	+	+	+	Blood-flecked mucus.
16	16	40	40	0	0	+	+	+	Yellow fecal mass.
17	12	1	0	0	1	+	+	+	Green muco-fecal.
18	23	31	5	26	0	+	+	0	Blood-flecked mucus.
19	24	4	1	0	3	+	+	+	Small bloody mucous.
20	12	12	12	0	0	+	+	+	Mucus and pus.
21	17	20	9	11	0	+	+	+	Blood-flecked mucus.
22	12	22	22	0	0	+	+	0	Blood-flecked mucus.
23	16	30	30	0	0	0	+	+	Green semi-liq. mucus.
24	14	18	18	0	0	0	+	+	Yellow semi-liq. mucus.
25	16	2	2	0	0	0	+	+	Green muco-fecal.
26	16	3	3	0	0	0	+	+	Muco-fecal.
27	20	8	8	0	0	0	+	+	Green muco-fecal.
28	20	7	7	0	0	0	+	+	Muco-fecal.
29	20	13	13	0	0	0	+	0	Yellow mucus.
30	19	2	2	0	0	0	+	+	Green offensive fecal.
31	15	3	2	1	0	0	+	+	Yellow liq. mass.
32	20	3	3	0	0	0	+	+	Muco-fecal.
33	24	34	0	0	34	0	+	+	Large liq. muco-fecal.
34	12	2	1	1	0	0	+	+	Green muco-fecal.
35	22	22	22	0	0	+	+	+	Viscid bloody mucus.
36	12	3	0	0	3	0	+	+	Large liq. muco-fecal.
37	21	41	41	0	0	0	+	+	Green muco-fecal.
38	17	6	4	0	2	0	+	+	Green mucus and pus.
39	14	2	2	0	0	0	+	+	Semi-solid mucous.
40	17	47	33	14	0	0	+	+	Large muco-fecal.
41	16	41	41	0	0	0	+	0	Mucous stool.
42	16	18	18	0	0	+	+	+	Blood-flecked mucus.
43	17	45	0	0	45	0	+	+	Yellow mucus.
44	16	33	33	0	0	0	+	+	Large muco-fecal.
45	12	60	60	0	0	0	+	+	Large soft fecal stool.
46	16	1	1	0	0	+	+	+	Mucous and bloody.
47	29	25	5	20	0	0	+	+	Light yellow feces.
48	17	6	5	1	0	+	+	+	Green bloody muco-fecal.
49	18	1	1	0	0	0	+	+	Watery brown and offensive.
50	18	0	0	0	0	0	+	+	Large offensive mucous.
51	12	11	11	0	0	0	+	+	Brown muco-fecal.
52	15	15	15	0	0	+	+	+	Blood-flecked mucus.
53	23	0	0	0	0	0	+	0	Yellow serum.
54	12	23	23	0	0	0	+	?	Brown-stained mucus.
55	12	4	0	0	4	0	+	+	Muco-fecal and curdy.
56	14	2	0	0	2	0	+	+	Green muco-fecal.
57	20	0	0	0	0	0	+	0	Curdy stool.
58	17	1	1	0	0	+	+	?	Bloody mucus.
59	12	2	2	0	0	+	+	0	Bloody mucus.
60	14	1	1	0	0	0	+	+	Green muco-fecal.

Clinical Case Number.	Plates Made.	Dysentery Colonies Isolated.	Fermenters of Mannit. "Harris."	Fermenters of Mannit. Bacillus "Y."	Non-fermenters of Mannit. ("Shiga.")	Blood in the Stool.	Mucus in the Stool.	Feces in the Stool.	Brief Description of the Stool.
61	12	18	0	18	0	0	+	?	Creamy pus and mucus.
62	12	3	3	0	0	0	+	?	Semi-solid green mucus.
63	12	2	2	0	0	0	+	0	Bloody mucus.
64	16	0	0	0	0	+	+	?	Green mucus.
65	12	2	2	0	0	0	+	0	Yellow serum.
66	12	1	0	0	1	+	+	?	Bloody mucus.
67	24	2	2	0	0	0	+	0	Yellow curdy mass.
68	14	1	0	0	1	+	+	0	Mucus with blood fleck.
69	12	18	18	0	0	+	+	0	Blood-flecked mucus.
70	12	12	12	0	0	0	+	?	Mucosa scraping.
71	6	70	70	0	0	+	+	0	Blood-flecked mucus.
72	24	0	0	0	0	+	+	0	Bloody mucus.
73	6	1	0	0	1	+	+	?	Blood-flecked mucus.
74	16	1	1	0	0	ɔ	+	+	Brown muco-fecal.
75	15	3	2	1	0	+	+	+	Muco-fecal, blood flecked.
76	19	8	0	0	8	ɔ	+	+	Green muco-fecal.
77	20	8	8	0	0	ɔ	+	0	Yellow mucus and pus.
78	24	3	3	0	0	0	+	+	Green muco-fecal.
79	22	5	2	3	0	0	+	+	Muco-fecal.

NOTES:

Nos. 1 to 67 inclusive are the cases obtained from Vanderbilt Clinic.
68 to 72 " " " " " " Post Graduate Hospital.
73 to 75 " " " " sent by Dr. La Fétra.
76 is a private case of Dr. Larkin (autopsy).
77 is a case from the Roosevelt Hospital.
78 and 79 are private cases sent by Dr. Schwerdtfeger.
Numbers 50, 53, 57, 64 and 72 are the negative cases.
Numbers 7, 8, 11, 13, 19 and 38 are cases in which both types ("Flexner-Harris" and "Shiga") were recovered from the stool.
Eleven (11) cases contained the "Shiga" type only.
Fifty-five (55) cases " " "Flexner-Harris" type either alone or associated with Bacillus "Y."
Six (6) cases " " "Shiga" and "Flexner-Harris" types in association.
One (1) case " " Bacillus "Y" only.

cultures varied considerably, and they bore no fixed relation to the "Flexner-Harris" organism. While it might form but a fraction of the entire number of dysentery colonies, it might again be the predominating bacillus.

The "Flexner-Harris" Bacillus in Normal Stools.—In view of the wide distribution of B. dysenteriae in the intestinal diseases of children a search was made to ascertain whether they might possibly be present in the intestine of normal children. For this purpose we employed the stools of normal milk-fed infants. The procedure was as fol-

lows: The rectum was first irrigated after which a dose of castor oil and rhubarb was administered. The first two free movements were examined. The method was to use the usual technique with the first stool, while from the second one from 3 to 6 drops of the bouillon suspension were carried into the plates. This modification was necessary to obtain plates with a fair number of colonies. From each case 50 to 100 plates were procured and several hundred colonies (up to 300) transplanted to the semi-solid jelly. By this means we succeeded in isolating a few colonies of the "Flexner-Harris" bacillus from the stools of two infants who were in perfect health.

REPORT OF MARTHA WOLLSTEIN, M.D., ASSISTED BY GRACE DEWEY, M.D.

From the Laboratory of the Babies' Hospital, New York.

During the three months extending from June 15th to September 15th there were studied by us 62 cases of diarrhea, which were examined with respect to the presence of Bacillus of Dysentery (Shiga) in the dejecta and the intestinal mucosa after death. The materials of our study were obtained from the Babies' Hospital, the N. Y. Foundling Hospital and in one instance from Dr. E. L. Coolidge. The children varied in age from six weeks to two years.

The specimens from the stools were taken in the following way: At the Babies' Hospital, when a case had been diagnosed as "diarrhea" in the ward, a characteristic stool was sent to the laboratory as soon as passed, and plates were poured at once. At the Foundling Hospital the cases in the ward for intestinal diseases were visited every morning, and suspensions from the fresh stools made in peptone water. These were carried to the laboratory and plated within half an hour. The children in the latter institution were more severely ill and the mortality rate was higher than was the case at the Babies' Hospital. This may be partly explained by the fact that, as the babies are boarded out in the tenements to paid nurses, they are returned to the hospital only when they become very ill. At the Babies' Hospital almost every case of diarrhea was studied.

Of the 62 cases the dysentery bacillus was isolated in 48 instances, that is 78 per cent. of all cases were positive for the bacillus. Numerically the cases occurred as follows: Babies' Hospital, 33; Foundling Hospital, 28; private practice, 1. Among the 33 cases studied from the Babies' Hospital 22, or 67 per cent., gave positive results; and of the 28 cases studied at the Foundling Hospital 25, or 89 per cent., gave positive results. The mortality of the cases yielding the dysentery bacillus was 55 per cent. at the Babies' Hospital and 78 per cent. at the Foundling Hospital.

The discharges varied considerably. Blood was present in a little more than one-third of all cases studied, namely in 22 instances and

among these the dysentery bacillus was found 19 times. Mucus in moderate or large quantity, in the absence of blood, was noted in 23 cases: among these 20 showed the presence of the bacillus. Mucus in small quantity, in the absence of blood, was present in 17 cases of which 9 gave the dysentery bacillus in culture. From this statement it will appear that movements containing much mucus are favorable for obtaining the bacillus, irrespective of the presence of blood in the discharges.

On the whole, the number of colonies of the dysentery bacillus present on the plates was not very numerous, though in one case they were almost the only variety present. In the cases containing much mucus, with or without blood, Bacillus dysenteriae was often found quite readily at the first "fishing"; but, when the case came under observation comparatively late in the disease (after the second week), it was hard to find even in stools containing blood.

Stools with small amounts of mucus, no blood, and a large amount of fecal matter, often necessitated fishings of very large numbers of colonies on successive days in order to find any dysentery bacilli, and the result on several occasions was but a single positive tube. An interesting point in this connection is that when such stools occur at the onset of a subsequently severe attack, Bacillus dysenteriae is found in them in comparatively large numbers, and increases as the stools become more mucous or bloody in character. On the other hand, if the attack is simply one of mild intestinal disturbance, without the appearance of any larger quantity of mucus at any time, the organisms are found in very small numbers or not at all. The same is true of those fecal stools containing a very small quantity of mucus which occur during the latter part of an attack of dysentery, or during convalescence. A good clinical history is important for the determination of these points.

The number of colonies of the dysentery bacillus transplanted, which represents the number of cultures obtained from a given case, varied from 1 to 25. All the colonies agreed in behaving on the litmus-mannite-agar medium as does the "Flexner-Harris" type of bacillus. In no instance was a colony of the "Shiga" type discovered.

The agglutination tests were made with the antidysenteric serum prepared in the horse and supplied by Dr. Flexner. The positive reactions were obtained with "Harris" serum in dilutions up to 1:3,000 and with the "Shiga" serum up to 1:400. There were some varia-

tions among the individuals isolated, in that certain of them proved relatively poor agglutinators.

Blood in sufficient quantity to suffice as a test for agglutination was obtained from 7 children giving positive and 2 giving negative bacteriological results.

I. Positive Cases.

3d	day,	positive	in	dilution	of	1-200,	1	case
6th	"	"	"	"	"	1-100,	1	"
6th	"	"	"	"	"	1-40,	1	"
7th	"	"	"	"	"	1-200,	1	"
2nd	"	negative	"	"	"	1-50,	1	"
4th	"	"	"	"	"	1-50,	1	"
10th	"	"	"	"	"	1-50,	1	"

II. Negative Cases.

5th	day,	negative	in	dilution	of	1-50,	1	case
6th	"	"	"	"	"	1-50,	1	"

Our experience in examining stools and scrapings from the intestinal mucosa in the same case convinced us that the dysentery organisms are at times more richly present in the intestine than in the discharges. Thus case 51 showed a small number of colonies in the stool and a large number in scrapings made from the rectum after death. Case 25 showed a moderately large number of colonies in the stool (24) and a much greater number in plates made from scrapings of the mucosa of the intestine. Case 29 was a failure until scrapings from the colic mucous membrane were examined. On the other hand three cases (5, 6, 18) were negative both in respect to stools and scrapings. Case 5 was first examined June 18. The stool was small and thin and contained a small amount of mucus. The autopsy was performed on July 15th and scrapings taken from the ileum and colon. Case 6 gave a stool containing a small quantity of mucus; the rectum was scraped after death. Case 18, stool showed very small quantity of mucus; rectum scraped after death.

We observed one instance of terminal infection in which a large number of colonies of the dysentery bacillus developed on the plates. The case (13) was that of a child of 5 months who was brought to the Babies' Hospital suffering from nephritis. Bloody discharges began 10 days after the child had entered the hospital. The case terminated fatally; no autopsy was permitted.

In one instance (Case 61) we obtained from a stool containing a

Clinical Case Number.	Number of Plates Made.	Dysentery Colonies Isolated.	Type of Colonies. "Harris."	Type of Colonies. "Shiga."	Blood in Stool.	Mucus in Stool.	Feces in Stool.	Brief Description of Stool.	Termination of Case.
1	6	16	All	o	+	+	+	Thin green	Death.
2	6	4	All	o	+	+	+	Yellow, small	Death.
3	6	3	All	o	+	+	+	Moderately large green	Not stated.
4	5	o	o	o	o	+	+	Small, green	Not stated.
5	15	o	o	o	o	+	+	Small, green; little mucus; much feces	Death.
6	10	o	o	o	o	+	+	Small, grayish-green; little mucus.	Death.
7	6	o	o	o	+	+	+	Large, yellow fecal; specks of blood; little mucus	Not stated.
8	4	4	All	o	+	+	+	Large, green	Not stated.
9	4	3	All	o	+	+	+	Small, thin, with much mucus and streaks of blood	Not stated.
10	5	3	All	o	+	+	+	Large, with much mucus and specks of blood, feces	Not stated.
11	7	2	All	o	o	+	+	Large, thin, green, with feces and much mucus	Death.
12	2	7	All	o	+	+	+	Small, with mod. mucus and streaks of blood	Not stated.
13	3	18	All	o	+	+	+	Small, chiefly blood and mucus	Death.
14	4	6	All	o	+	+	+	Small, green, with much mucus and streaks of blood	Death.
15	8	3	All	o	o	+	+	Large, white and green, much mucus	Not stated.
16	4	18	All	o	+	+	o	Small; blood and mucus	Recovery.
17	16	2	All	o	o	+	+	Large, thin, green-brown, much mucus	Not stated.
18	12	o	o	o	o	+	+	Large, green; very little mucus	Death.
19	9	o	o	o	o	+	+	Large, green; very little mucus	Death.
20	6	7	All	o	+	+	+	Green; much feces, little blood and mucus	Recovered.
21	12	2	All	o	o	+	+	Small, yellow; mod. mucus	Not stated.
22	8	o	o	o	o	+	+	Green; much feces, little mucus	Not stated.
23	12	5	All	o	+	+	+	Green; mod. mucus, little blood	Death.
24	10	o	o	o	o	+	+	Large, green; fecal, little mucus	Recovered.
25	14	24	All	o	o	+	+	Small, green; mod. mucus	Death.
26	6	6	All	o	o	+	+	Large, green; fecal, little mucus	Recovered.
27	10	1	All	o	+	+	+	Small, green; mod. mucus, streaks of blood	Not stated.
28	7	o	o	o	o o	+	+	Thin, green and yellow; much feces; little mucus	Recovered.
29	10	3	All	o		+	+	Thin, green and yellow; much feces; little mucus	Death.
*30	10	o	o	o	o	+	+	Dark green; much feces and mucus	Recovered.
31	9	4	All	o	o	+	+	Large green; much feces and mucus	Death.
32	4	6	All	o	o	+	+	Large, thin, green; much feces, little mucus	Not stated.

* Diarrhea followed eating of sausage and lasted five days.

Clinical Case Number.	Number of Plates Made.	Dysentery Colonies Isolated.	Type of Colonies.		Blood in Stool.	Mucus in Stool.	Feces in Stool.	Brief Description of Stool.	Termination of Case.
			"Harris."	"Shiga."					
33	7	10	All	0	0	+	+	Thin, green; much feces, little mucus.	Death.
34	4	3	All	0	0	+	+	Small green; little feces and mucus	Not stated.
35	10	8	All	0	0	+	+	Small, green, yellow; mod. mucus	Not stated.
36	12	3	All	0	0	+	+	Large, thin, green; mod. mucus	Not stated.
37	8	4	All	0	0	+	+	Small, green; mod. mucus	Not stated.
38	6	7	All	0	0	+	+	Small, green; little mucus	Recovered.
39	4	5	All	0	0	+	+	Large, green; much mucus, little feces	Not stated.
40	14	0	0	0	0	+	+	Yellow and green; much feces, little mucus	Death.
41	10	1	All	0	+	+	+	Green; much mucus, speck of blood	Not stated.
42	6	1	All	0	+	+	+	Thin, green; much mucus, flecks of blood	Not stated.
**43	18	4	All	0	0	+	+	Small, green; little mucus, feces	Not stated.
44	5	6	All	0	0	+	+	Green; much mucus and feces	Death.
45	16	2	All	0	0	+	+	Large, brown; mod. mucus and feces	Not stated.
46	16	3	All	0	0	+	+	Large, green; much mucus, mod. feces	Not stated.
47	10	6	All	0	0	+	+	Large, brown; mod. mucus, mod. feces	Not stated.
48	9	2	All	0	0	+	+	Small, yellow; much mucus and feces	Not stated.
49	14	1	All	0	0	+	+	Green; fecal, little mucus	Death.
50	8	1	All	0	0	+	+	Small, thin, green; mod. mucus and feces	Not stated.
51	18	3	All	0	0	+	+	Thin, green; much mucus and feces	Death.
52	10	3	All	0	0	+	+	Large green; much mucus and little feces	Not stated.
53	5	3	All	0	—	—	—	———	Death.
54	4	3	All	0	0	+	+	Small, yellowish green; mod. mucus and feces	Not stated.
55	5	3	All	0	+	+	+	Small, colorless; much mucus, streaks of blood, little feces	Not stated.
56	2	8	All	0	0	+	+	Small, green; much mucus, mod. feces	Not stated.
57	18	2	All	0	0	+	+	Small, greenish; little mucus and feces	Not stated.
58	12	3	All	0	+	+	+	Large, yellow; much mucus, few streaks blood, mod. feces	Not stated.
59	3	0	0	0	+	+	+	Small, green; mod. mucus, little feces, few streaks of blood	Death.
60	8	25	All	0	—	—	—	———	Death.
61	10	0	0	0	0	+	+	Large, yellowish brown; mod. mucus, much feces	Not stated.
62	12	0	0	0	+	+	+	Thin, yellow; much mucus, streaks of blood, little feces	Not stated.

**Sets of plates made two weeks previously failed to yield B. dysenteriæ.
Cases 53 and 60.—Used scrapings of intestinal mucosa obtained at autopsy.
Case 61.—Non-motile, alkali-producing bacillus isolated.

moderate quantity of mucus a non-motile bacillus which conducted itself in a manner similar to the "Shiga" type of dysentery bacillus, but there was strong alkali formation in litmus milk after a primary acid production. The bacillus did not agglutinate with "Shiga" antidysenteric serum.

The foregoing table gives in numerical order the cases which we studied and the results of the bacteriological examination.

REPORT OF FREDERICK P. GAY, M.D., ASSISTED BY E. McD. STANTON, M.D.

The stools from cases of infantile diarrhea which have come into our hands for bacteriological investigation during the months of June, July, August and September—our working period having extended from the end of June to the middle of September—were obtained from two sources. The larger number of specimens was sent in by the New York Health Department, the cases from which they had been obtained being observed clinically and the specimens collected by the district medical inspectors in their rounds of the tenement districts. The smaller number of specimens was obtained from the children's wards of Bellevue Hospital through the courtesy of Drs. Mabon and Norrie and the resident staff. The examination of the collected material was carried out in the Bacteriological Laboratory of the New York University and Bellevue Hospital Medical College. We wish to thank the many persons who directly and indirectly assisted us for their interest and courtesies.

Owing to the nature of the circumstances affecting the material with which we operated, the most satisfactory bacteriological results were obtained with the specimens supplied from the wards of Bellevue Hospital. From a clinical standpoint the cases yielding the dejecta were similar in the hospital and the tenement districts, with the possible difference that the cases which found their way into the hospital were often of longer duration than in the latter quarter. But the most important difference, so far as our studies were concerned, consisted in the fact that complete fresh stools could be obtained from the hospital while, through the unavoidable nature of the situation, we had to content ourselves with small portions of mucus, etc., which were chosen hurriedly by the medical inspectors and sent us suspended in normal saline solution and which reached us some hours often after being collected. Seeing that this latter material was obtained from napkins which had not been sterilized and had often been kept under careless conditions for hours, it was, theoretically, unpromising for the purposes of our investigation. It is, therefore, not surprising that the specimens from a large number of the cases of diarrhea occurring in the tenement district were found to be grossly contaminated with air and other foreign bacteria.

The material from Bellevue Hospital, on the other hand, was received on sterile pads almost immediately after its passage and the plates made from it were completed frequently within half an hour after the movement had taken place. Besides this we could observe and record the character of the stool and make a deliberate selection of those portions which offered the best opportunities for successful bacteriological study.

The method which we pursued in separating the bacillus of dysentery was essentially that described by Vedder and Duval. Several suspensions were made of the mucus from various parts of the stool and from these suspensions transfers of a varying number of loops were made to fluid agar-agar which was acid 1.5 per cent. to phenolphthalein. Frequently the mucus particles were washed in sterile salt solution before suspension to remove the excess of colon bacilli which are contained in the fecal part of the stool. On an average about 20 agar-agar plates were made; but in some unpromising cases as many as thirty or forty were prepared. In general the most satisfactory plates were found to be the rather thickly seeded ones; *e.g.*, those containing from 200 to 300 colonies. After the lapse of the twenty-four hour incubation period and the marking of the superficial colonies, subsequently developing surface colonies of the colon bacillus type were taken directly into 1 per cent. glucose agar, or, better still, into Hiss' semi-solid gelatine-agar medium which has the advantage of showing motility and gas production within a few hours after inoculation and incubation. All non-motile, non-gas-forming bacilli were then grown in litmus milk and such of them as showed the slight acid production in 24 hours, characteristic of the growths of B. dysenteriae, were tested for agglutination with two antidysenteric horse's sera representing the "Shiga" and the "Flexner-Harris" strains of the bacillus of dysentery. The dysentery bacilli agglutinate with both sera, but relatively better with the serum of the type to which the bacillus belongs.

The stools which yielded B. dysenteriae did so readily, as a rule, on the second or third "picking," but we met with a few stools in which we succeeded only after three or four "pickings" in obtaining a single colony of the organism. The small proportion of dysentery bacilli occurring in the latter stools may be gathered from the fact that as many as 100 to 200 colonies were at times transplanted in order to obtain this imperfect result.

Of the microorganisms growing in cultures the ones frequently met with—excluding B. dysenteriae—in our plates were B. coli communis,

B. fecalis alkaligenes, B. acidi lactici, and the streptococcus. A few specimens which contained large numbers of streptococci failed to yield us the dysentery bacillus.

Several bacilli of the colon group and certain bacilli resembling B. fecalis alkaligenes were encountered which gave positive agglutination sometimes with one, sometimes with the other of the anti-dysenteric sera of the horse; but we met with no organism except the dysentery bacillus which reacted to both types of serum.

We were successful in recovering the dysentery bacillus from 20 cases of infantile diarrhea. Of the 20 cases 18 contained organisms of the "Flexner-Harris" type and 2 organisms of the "Shiga" type. In no instance were the two types of organism isolated from the same case.

In several instances the freshly isolated cultures of B. dysenteriae failed to agglutinate with the anti-dysenteric sera; but these cultures all reacted positively after repeated sub-culturing.

We met with certain cultures which resemble the dysentery bacillus in all respects, but which behaved in a non-characteristic manner upon litmus-milk. These cultures produced the initial acidity and returned the color of the milk to that of the control. But later they gave rise to a second acid-production which was permanent. We have not investigated farther, because of lack of time, the finer points of distinction between this organism and the bacillus of dysentery.

MATERIAL SUPPLIED BY NEW YORK HEALTH DEPARTMENT.

Of the 28 stools examined from this source the bacillus of dysentery was isolated in 7 instances or in 25 per cent. We have tabulated the cases from which the specimens were obtained with reference to the reported nature of the stools:

Of 12 stools showing little mucus and no blood two (2) gave B. dysenteriae.

Of 12 stools showing moderate quantities of mucus and no blood five (5) gave B. dysenteriae.

Of 4 stools showing large quantities of mucus and some blood none gave B. dysenteriae.

At the first glance there is something contradictory in these results, for it has been stated by Duval and Bassett that the stools in which blood and mucus were contained most easily yield B. dysenteriae in cultures. The reason for this unexpected result becomes evident when we look at the contaminations which were met with in many of this

class of cases and which are to be ascribed to the unfavorable conditions under which the collection of the specimens was made.

MATERIAL SUPPLIED BY BELLEVUE HOSPITAL.

Of the 20 cases examined from this source the bacillus of dysentery was found in 13 or in 65 per cent. A tabulation of the cases and results follow:

Of 1 stool showing little mucus and no blood no successful result.

Of 3 stools showing little mucus and blood three (3) gave B. dysenteriae.

Of 5 stools showing moderate quantity of mucus and no blood five (5) gave B. dysenteriae.

Of 6 stools showing large quantity of mucus and no blood three (3) give B. dysenteriae.

Of 5 stools showing large quantity of mucus and some blood two (2) gave B. dysenteriae.

Our results were assisted in this group of cases by the fact that it was often possible to secure a second or third specimen of the discharges from a given case; and thus it happened that after failure with the first specimen a subsequent one, presenting the same naked-eye appearance as the first, would yield B. dysenteriae. In several of the negative cases unusual conditions prevailed which possibly accounted, in part, for the failures. In one case B. pyocyaneus overgrew the plate and suppressed other organisms; and in another B. proteus behaved in the same manner. One of the stools was well formed, two were watery with a trace only of mucus, and two stools contained enormous numbers of streptococci.

Autopsies were held on five of the fatal cases. In one case showing generalized tuberculosis the colon showed no lesions although the bacillus of dysentery was obtained during life from the discharges; in two instances the colon was congested and showed hemorrhagic points; two cases presented extensive ulcerative colitis. In the last two cases the ileum showed ulcers in the one and the base of the appendix ulceration and gangrene in the other. Cultures made from the colon of the last two cases gave B. dysenteriae.

Very few opportunities were presented for the study of the agglutinative power over dysentery bacilli of the blood of infants ill of diarrhea. The very few specimens of blood which we tested reacted variously—some positively in dilutions up to 1:20, some negatively in dilutions of 1:10. But as our data are very imperfect and incomplete and little

Clinical Case Number.	Number of Plates Made.	Dysentery Colonies Isolated.	Types of Colonies. "Harris."	Types of Colonies. "Shiga."	Blood in Stool.	Mucus in Stool.	Feces in Stool.	Brief Description of Stool.	** Source of Specimen.
1	15	2	2	0	0	+	+	Small quantity mucus supplied	N.Y.H.D.
2	18	6	6	0	+	+	+	Greenish-yellow	N.Y.H.D.
3	18	0	0	0	0	+	+	Greenish with trace of blood	N.Y.H.D.
4	18	0	0	0	0	+	+	Yellow soft feces	N.Y.H.D.
*5	—	—	—	—	—	—	—	———	N. Y. D.
*6	—	—	—	—	—	—	—	———	N.Y.H.D.
7	18	2	2	0	0	+	+	Greenish with curds; little mucus	N.Y.H.D.
8	16	0	0	0	?	+	?	Specimen in sterile bottle	N.Y.H.D.
9	16	0	0	0	0	+	+	Greenish-yellow curds	N.Y.H.D.
*10	—	—	—	—	—	—	—	———	N.Y.H.D.
11	18	8	8	0	0	+	?	Rec'd in sterile salt sol.	N.Y.H.D.
12	18	3	3	0	0	+	?	Rec'd in sterile salt sol.	N.Y.H.D.
13	16	0	0	0	0	+	+	Rec'd in sterile salt sol.	N.Y.H.D.
*a*14	21	0	0	0	+	+	0	Dried mucus; trace of blood	N.Y.H.D.
15	18	0	0	0	0	+	+	Rec'd in salt sol.	N.Y.H.D.
16	15	0	0	0	+	+	+	Bloody mucus on rectal tube	B. H.
17	16	0	0	0	0	+	+	Rec'd in salt sol.	B. H.
18	18	1	1	0	0	+	?	Greenish; much mucus	B. H.
19	16	7	7	0	0	+	?	Yellow-green; consid. mucus	B. H.
*c*20	—	—	—	—	—	—	—	———	———
21	16	0	0	0	0	+	+	Green ; semi-fluid	N.Y.H.D.
22	16	0	0	0	0	+	+	Rec'd in salt sol.	N.Y.H.D.
23	15	0	0	0	0	+	+	Rec'd in salt sol.	N.Y.H.D.
*24	15	0	0	0	0	+	+	Yellow curds rec'd on paper	N.Y.H.D.
*25	—	—	—	—	—	—	—	———	B. H.
*b*26	9	4	4	0	0	+	+	Green; little mucus, feces	B. H.
27	9	0	0	0	0	+	+	Formed with trace of mucus; much feces	B. H.
28	11	2	2	0	0	+	+	Large green curds; consid. mucus	B. H.
*b*29	40	0	0	0	+	+	+	Large stool in chamber	N.Y.H.D.
*b*30	15	2	2	0	+	+	?	Small, foul, greenish ; little mucus and blood	B. H.
*b*31	20	5	5	0	+	+	?	Small, with much mucus and trace of blood	B. H.
32	15	0	0	0	+	+	?	Fluid, green; trace of blood.	B. H.
33	40	54	54	0	0	+	+	Small, green, muco-purulent	B. H.
34	16	0	0	0	0	+	+	Rec'd in salt sol.	N.Y.H.D.
35	21	0	0	0	0	+	+	Green ; consid. mucus and feces	B. H.

* Cases 5, 6, 10, 25 are not included in reports as illness of under-assistant prevented them from being worked out completely.

** N.Y.H.D.=New York Health Department; N. Y. D.=New York Dispensary; B. H. =Bellevue Hospital; G. S. D.=Good Samaritan Dispensary.

a. Case 14 showed large numbers of cocci.

b. Case 26 at autopsy showed congestion and hemorrhages in intestine; cultures from colon gave colonies of "Flexner-Harris" type of B. dysenteriæ. Case 30 at autopsy showed extensive ulcerations of ileum and colon; mesenteric glands enlarged and hemorrhagic; cultures from ileum and from colon yielded B. dysenteriæ (Flexner-Harris), and from mesenteric glands B. coli com.; Case 31 at autopsy showed ulcerative colitis and ulceration and gangrene of appendix.

c. Editorial Note.—In preparing this table from the "Bacteriological Reports" No. 20 was found missing from the series.—S. F.

Clinical Case Number.	Number of Plates Made.	Dysentery Colonies Isolated.	Types of Colonies. "Harris."	Types of Colonies. "Shiga."	Blood in Stool.	Mucus in Stool.	Feces in Stool.	Brief Description of Stool.	** Source of Specimen.
36	15	0	0	0	0	+	?	Watery brown on sterile pad	B. H.
37	16	0	0	0	0	+	+	Rec'd in sterile tube	N.Y.H.D.
*a*38	35	6	6	0	+	+	+	Bloody matter with feces on rectal tube	B. H.
39	20	0	0	0	+	+	+	Dried specimen	N.Y.H.D.
40	19	1	1	0	0	+	+	Green, large; much mucus and feces	B. H.
41	22	1	1	0	+	+	+	Small, brownish; mod. amt. mucus; little blood	B. H.
42	30	0	0	0	0	+	+	Greenish curds	N.Y.H.D.
43	32	1	1	0	0	+	+	Feces and large curds; mod. amt. mucus	B. H.
44	24	2	0	2	+	+	0	Small quantity of mucus and blood	B. H.
45	20	8	0	8	0	+	+	Greenish-yellow; much mucus and feces	G. S. D.
*b*46	24	0	0	0	+	+	+	Yellow-green; much mucus; trace blood	G. S. D.
*b*47	24	0	0	0	0	+	+	Whitish feces with mucus	G. S. D.
48	25	1	1	0	0	+	0	Muco-purulent	B. H.
49	17	1	1	0	0	+	+	Rec'd in rectal tube	G. S. D.
*b*50	17	0	0	0	0	+	+	Greenish curds; consid. mucus	B. H.
*b*51	25	0	0	0	0	+	+	Greenish-yellow; much mucus	B. H.
*b*52	28	0	0	0	0	+	+	Greenish; mod. amt. mucus, feces	G. S. D.
*b*53	33	0	0	0	0	+	+	Rec'd in rectal tube	G. S. D.

** N.Y.H.D.=New York Health Department; N. Y. D.=New York Dispensary; B. H.=Bellevue Hospital; G. S. D.=Good Samaritan Dispensary.

a. This case was plated three times and always contained an organism which overgrew the plates in 48 hours. The successful isolation was made by taking off colonies from some plates at the end of 24 hours.

b. Cases 46, 47, 50, 51, 52, 53 showed large numbers of cocci.

can be made out from them of the duration and severity of the symptoms, we do not regard them as of sufficient value to include in this report.

The conclusions which we here draw from our study, the main facts and features of which are here presented, is that B. dysenteriae can be found in all cases possibly of infantile diarrhea in which the discharges contain mucus, whether or not it is accompanied by blood. The percentage of cases in which positive results occur will depend upon certain conditions inherent in the material or operating from without. Besides the factors of freshness and cleanliness in the stools and the reaction of the culture medium used for plating which are to be regarded, we have found, as unfavorable, watery condition, much feces and large number of cocci in the discharges.

REPORT OF LOUISE CORDES, M.D.,

Pathologist to the New York Infirmary for Women and Children.

During the summer months stools from 51 cases of gastro-intestinal disturbance in infants and children were examined in the Laboratory of the New York Infirmary for Women and Children, for the presence of Bacillus dysenteriae.

Material was obtained from cases treated at the Nursery and Child's Hospital and the New York Infirmary for Women and Children; one case was seen in the Babies' Hospital dispensary.

The Infirmary series included dispensary and outpractice as well as hospital cases.

Stools from 10 cases were obtained from the Nursery and Child's Hospital, 9 from the New York Infirmary and 31 from the dispensary and out-patient department of the Infirmary.

The stools were not selected, material from all cases of gastro-intestinal disorder, even those showing the mildest symptoms, having been examined.

The material was in a great many cases obtained fresh and plated at once; in some of the outdoor cases stools were brought from one to two hours after being passed, but not later. The Bacillus dysenteriæ was found in the stools of 26 cases—or in 51 per cent. Two cases of 5 and 10 years respectively are included in the list, the remainder being under 2½ years old.

The ages of the children whose stools were found to contain the Bacillus dysenteriae ranged as follows:

Under 6 months	4
From 6-12 months	5
From 12-18 months	5
From 18 months to 2½ years	10
Over 5 years	2

In the cases giving positive results, the character of the stools was as follows: Soft greenish-yellow feces with much mucus and no blood (in one of these cases there was a history of blood), 14; green feces with little or a moderate amount of mucus and no blood, 6; green or

yellow feces without mucus or blood, 2; brownish-yellow liquid without mucus or blood (in this case there had been a previous attack during which the stools were not watery, but consisted of green and yellow feces and mucus), 1; green feces, mucus and blood (two of the stools in this series contained curds and one, undigested food), 3.

The negative stools showed the following characters: Green feces with much mucus and no blood, 1; green or yellow feces with a moderate amount of mucus and no blood, 6; green or green and yellow feces with little mucus and no blood, 6; green or green and yellow feces with much or a moderate amount of mucus and blood, 5; greyish-green and yellow, or green feces no mucus, no blood (two of these stools contained undigested food and one, curds), 7.

The frequency of the stools in the cases in which Bacillus dysenteriæ was found varied considerably; there were, in 24 hours,

4-6	stools	in	6	cases
5-10	"	"	6	"
6-12	"	"	1	"
7	"	"	2	"
10-12	"	"	8	"
12-15	"	"	1	"
15-20	"	"	2	"

In the negative cases the frequency of the stools was:

12-20	in	1	case
10 or 10-12	in	4	cases
6-8	in	2	cases
5-7	"	4	"
3-5	"	8	"
2-5	"	3	"
2-3	"	3	"

In 25 stools the acid type of Bacillus dysenteriae was found; the alkaline type was isolated from one case.

Agglutination with the anti-dysenteric horse serum (Harris) was positive in dilutions of 1-3000 or 1-3500 with the bacillus of the "Flexner-Harris" type obtained from 6, in a dilution of 1-2000 in 12, in 1-1000 in 7 cases. These organisms showed agglutination with the "Shiga" anti-dysenteric serum in dilutions of 1-200 or 1-500 and in 1 case in 1-1000.

The bacillus of the alkaline (Shiga) type isolated from one case gave a positive reaction with the "Shiga" anti-dysenteric serum in a dilution of 1-7500 and with the "Harris" serum in 1-2000.

No. of Case.	No. Plates Made.	Total No. of Colonies Transplanted.	Number of Colonies of B. Dysenteriæ.	Type of Bacilli.		Blood in Stool.	Mucus in Stool.	Feces in Stool.	Description of Stool.	Agglutination.		Source of Material.
				"Harris."	"Shiga."					Positive.	Negative.	
1	12	60	3	3	0	0	+	+	Solid green and yellow; mod. mucus	———	———	B.H.D.
2	8	—	4	4	0	+	+	+	Semi-solid green curds; much mucus	1:50		N.C.H.
3	16	—	0	—	—	+	+	+	Semi-solid green; mod. mucus, very little blood	1:50		N.C.H.
4	12	—	0	—	—	0	+	+	Pasty, brownish-yellow		1:50	N.C.H.
5	4	—	0	—	—	0	+	+	Yellow; pasty with mod. mucus		1:50	N.C.H.
6	8	—	0	—	—	+	+	+	Green-yellow, semi-solid; little blood	1:50		N.C.H.
7	4	—	0	—	—	0	+	+	Green, semi-solid; little mucus			N.C.H.
8	8	—	0	—	—	0	+	+	Green, semi-solid; mod. mucus		1:50	N.C.H.
9	12	50	4	4	—	+	+	+	Soft, yellow; much mucus, little blood		1:50	N.C.H.
10	12	—	—	—	—	+	+	+	Soft, green and yellow; little blood		1:50	N.C.H.
11	12	—	0	—	—	0	0	+	Soft feces		1:50	N.C.H.
12	12	—	0	—	—	0	+	+	Pasty, green; mod. mucus		1:50	N.Y.I.
13	8	—	0	—	—	0	0	+	Semi-solid		1:50	N.Y.I.
14	8	—	0	—	—	0	+	+	Semi-solid; very little mucus		1:50	N.Y.I.
15	16	75	8	8	0	0	+	+	Green and yellow, semi-solid; much mucus	1:50		N.Y.I.
16	12	82	2	2	0	0	+	+	Green, yellow; little mucus		1:50	N.Y.I.
17	16	—	0	—	—	0	0	+	Semi-liquid, green and yellow		1:50	N.Y.I.
18	12	25	1	1	0	0	0	+	Soft, yellow green		1:50	N.Y.I.
19	8	—	0	—	—	0	+	+	Soft, green; very little mucus		1:50	N.Y.I.
20	12	—	0	—	—	0	+	+	Soft, green and yellow; trace of mucus		1:50	N.Y.I.
21	8	26	8	8	0	0	+	+	Soft, yellow; consid. mucus		1:50	
22	16	65	5	5	0	0	+	+	Soft, yellow; consid. mucus	———	———	N.Y.I.
23	12	—	0	—	—	0	0	+	Soft, green and yellow		1:50	N.Y.I.
24	8	—	0	—	—	0	+	+	Soft, green; mod. mucus		1:50	N.Y.I.
25	8	32	3	3	0	0	+	+	Soft, yellow, green; little mucus		1:50	N.Y.I.
26	8	—	0	—	—	0	0	+	Soft, green and yellow		1:50	N.Y.I.
27	8	—	0	—	—	0	+	+	Semi-solid, green and yellow; mod. mucus		1:50	N.Y.I.
28	8	65	6	6	0	0	+	+	Soft green, consid. mucus	1:50		N.Y.I.
29	8	28	1	1	0	0	+	+	Soft, green and yellow; little mucus		1:50	N.Y.I.
30	8	137	2	2	0	0	+	+	Soft, green, yellow; consid. mucus	———	———	N.Y.I.
31	8	61	3	3	0	0	+	+	Soft, green curds; consid. mucus	———	———	N.Y.I.
32	8	—	0	—	—	0	+	+	Soft, green; little mucus		1:50	N.Y.I.

B.H.D.=Babies' Hospital Dispensary. N.C.H.=Nursery and Child's Hospital. N.Y.I. =New York Infirmary.

No. of Case.	No. Plates Made.	Total No. of Colonies Transplanted.	Number of Colonies of B. Dysenteriæ.	Type of Bacilli.		Blood in Stool.	Mucus in Stool.	Feces in Stool.	Description of Stool.	Agglutination.		Source of Material.
				"Harris."	"Shiga."					Positive.	Negative.	
33	16	150	3	3	0	0	0	?	Yellow and watery (bit of gauze plated)		1:50	N.Y.I.
34	8	27	5	5	0	0	+	+	Soft, green, yellow; consid. mucus		1:50	N.Y.I.
35	12	22	2	0	2	0	+	+	Soft, yellow, brown; little mucus		1:50	N.Y.I.
36	8	130	3	3	0	0	+	+	Semi-solid; little mucus	1:50		N.Y.I.
37	8	140	4	4	0	+	+	+	Soft, yellow; much mucus, trace of blood		1:50	N.Y.I.
38	8	—	0	—	—	0	+	+	Soft, yellow; undigested food; very little mucus		1:40	N.Y.I.
39	12	41	1	1	0	+	+	+	Soft, green; consid. mucus	1:50		N.Y.I.
40	8	166	5	5	0	0	+	+	Semi-solid, green; consid. mucus	1:50		N.Y.I.
41	12	15	2	2	0	0	+	+	Soft, yellow; undigested food, consid. mucus		1:40	N.Y.I.
42	16	—	0	—	—	0	+	+	Soft, green; much mucus		1:40	N.Y.I.
43	12	—	0	—	—	0	+	+	Soft, green; much mucus		1:50	N.Y.I.
44	12	—	0	—	—	0	0	+	Semi-solid, greenish-yellow		1:40	N.Y.I.
45	12	75	2	2	0	+	+	+	Soft, greenish; much mucus, little blood		1:40	N.Y.I.
46	8	—	4	4	0	0	+	+	Soft, yellow; undig. food, much mucus	1:50		N.Y.I.
47	8	47	6	6	0	+	+	+	Soft, green and yellow; much mucus		1:40	N.Y.I.
48	12	—	0	—	—	0	+	+	Semi-fluid, green; mod. mucus		1:50	N.Y.I.
49	12	—	0	—	—	0	0	+	Soft, green, yellow		1:50	N.Y.I.
50	8	58	3	3	—	0	+	+	Semi-fluid, brown; mod. mucus	1:50		N.Y.I.
51	12	90	14	14	—	0	+	+	Semi-solid, green, yellow; much mucus		1:50	N.Y.I.

B.H.D.=Babies' Hospital Dispensary. N.C.H.=Nursery and Child's Hospital. N.Y.I. =New York Infirmary.

The blood of 46 cases, 22 of which yielded the Bacillus dysenteriae was tested with the "Flexner-Harris" and "Shiga" types of the dysentery bacillus in a dilution of 1-50. Of the 22 cases in which the bacillus was observed, 10 gave a positive reaction on the 4th to the 24th day of the disease; 12 failed to give a reaction, 11 of these having been tested on the 2nd to the 8th day of the disease and 1 on the twelfth day. A reaction was obtained in 3 negative cases.

The blood in the 22 negative cases, in which no reaction was obtained, was examined as follows:

2nd	day of the disease	3 cases
3rd	" " " "	1 "
7th	" " " "	2 "
8th	" " " "	1 "
9th	" " " "	1 "
10th	" " " "	3 "
11th	" " " "	2 "
14th	" " " "	2 "
15th	" " " "	1 "
18th	" " " "	1 "
25th	" " " "	1 "
3rd	week " " "	1 "
6th	" " " "	1 "
2d	month " " "	1 "

In those cases in which the stools were plated, more than one hour after they were passed, the following results are shown:

1½ hours after	3	Positive 2 Negative 1
2 hours after.....	8	All negative

The table expresses in brief form the main facts of my study.

REPORT OF W. W. WAITE, STUD.MED.

My report is based upon the bacteriological examination of 47 cases of diarrhea in children. The examinations were conducted in the Pathological Laboratory of the Johns Hopkins University. The specimens were drawn chiefly from the dispensary of the Johns Hopkins Hospital. Of the 47 cases studied 40 were supplied from the dispensary and 7 from the private practice of physicians in Baltimore. For the latter I wish to thank Drs. Booker and Thayer; and for the former, Dr. Amberg.

The report is based chiefly upon the results of my own examinations but as I had, during a short period, the valuable help of Mr. Shorer, who was detached from New York in order to bring me assistance, I wish to acknowledge the great aid that he rendered me. He brought into the work the advantage of improvements in method of isolating the bacillus with which the richer results of the investigation in New York and elsewhere had been achieved. Although he studied a very small number of cases during his stay in Baltimore his results are striking and noteworthy and have been indicated in the accompanying table.

I am confident that at the beginning of the summer I made the serious mistake of attempting to study too large a number of cases; and as the facilities for carrying on the study under the most favorable conditions had not then been completed, my results are less complete than I wish. But I am giving the records as I have them and shall comment no further upon the number of failures to secure the bacillus of dysentery which they indicate. It remains, however, for me to add that from two cases in which I failed to find the bacillus this organism was afterwards isolated by Dr. Bassett at the Wilson Sanitarium to which institution the children were taken for treatment.

Of the 47 cases studied bacteriologically 19 yielded the bacillus of dysentery, or, stated in percentages, in 40 per cent. of the cases that organism was isolated in cultures. The type of bacillus found was chiefly the "Flexner-Harris" organism, although in two instances the "Shiga" type was obtained. In no instance was a mixture of the two types met with.

For the most part the number of colonies of dysentery bacilli isolated

was small, although in a few instances the number was strikingly large. Thus in cases 44 and 46, 30 to 50 per cent. of the transplanted colonies proved to be that organism. The table states in the positive cases the number of colonies transplanted from the plates and the number of tubes of the dysentery bacillus which were secured from them.

The methods which I pursued in this study were, until Mr. Shorer's visit, those laid down by Vedder and Duval; and the identification of the bacilli as those of dysentery was made by the tests now usually employed. The absence of gas-formation in sugar media, the litmus-milk reaction, the appearances of the colonies, etc., upon the ordinary culture media and finally the agglutination reactions with anti-dysenteric horses' serum were all observed and noted. For the differentiation of the two types of bacilli the litmus-mannite-agar-agar of Lentz was used. After Mr. Shorer had introduced me to the use of Hiss' semi-solid jelly for the more ready separation of colonies of B. coli communis and some other bacilli from those of the dysentery bacillus I continued to employ in my later work that method of isolating the last named organism from the plates.

A scrutiny of the table will show that in my work I had the advantage of securing material for plating in a fresh condition, as the specimens were taken for me at the dispensary in rectal tubes. On the other hand, this method of securing specimens for bacteriological examination often precluded the study of the contents of the higher bowel, which fact should be considered in interpreting my results. In this connection it is proper to draw attention to the uniformly successful efforts in obtaining the bacillus of dysentery from cases in private practice where natural discharges were used for the plating.

The manner of securing the specimens was such as to make the question of the presence or absence of blood in the natural discharges very difficult to answer. The histories given by mothers in dispensary practice are very unreliable upon such points and, unfortunately, even the most careful insertion of the rectal tube will often be followed by a slight abrasion of the mucous membrane which leads to small bleedings. We have tried to eliminate this factor in our descriptions of the specimens examined, but with doubtful success. On the other hand, mucus is readily obtained by the tube method and cannot be held to bear any close relationship with the amount of mucus which might be present in these pathological cases in the natural discharges. As one glances over the table he is struck with the almost constant presence of mucus and feces in the specimens examined and the far less frequent presence of blood. For example, feces are encountered in all cases but one,

No. of Case.	No. Plates Made.	No. of Colonies Transplanted.	No. of Colonies of B. Dysenteriæ.	Type of Bacilli.		Blood in Stool.	Mucus in Stool.	Feces in Stool.	Description of Material Used.	Notes.
				"Harris."	"Shiga."					
1	10	47	4	4	0	+	+	+	Obtained by tubing; thin and gray	A
2	10	—	0	—	—	0	+	+	Obtained by tubing; thin and clear	A
3	12	—	0	—	—	+	+	+	Obtained by tubing; dark and green	A
4	10	—	0	—	—	+	?	+	Obtained by tubing; dark, reddish-brown	A
5	10	45	5	5	0	0	+	+	Obtained by tubing; thin, greenish-yellow	A
6	10	—	0	—	—	0	0	+	Obtained by tubing; thin and yellow	A
7	10	—	0	—	—	0	+	+	Obtained by tubing; mucus	
8	18	—	0	—	—	0	+	+	Obtained by tubing; dark brown, fecal and mucus	A
9	8	—	0	—	—	+	+	+	Obtained by tubing; pale mucus	A
10	8	—	0	—	—	0	+	+	Obtained by tubing; thin and brown	A
11	10	—	0	—	—	0	+	+	Obtained by tubing; thin and clear	B
12	10	20	1	1	0	0	+	+	Obtained by tubing; yellow mucus	A
13	12	—	0	—	—	0	+	+	Obtained by tubing; thin, greenish-yellow	B
14	18	79	3	3	0	+	+	+	Obtained on napkin; pasty, brownish yellow	C
15	12	—	0	—	—	0	+	+	Obtained by tube; thin, greenish mucus	A
16	9	—	0	—	—	+	+	0	Obtained by tube; mucus and little blood	A
17	10	—	0	—	—	0	+	+	Obtained by tube; small and pus-like	A
18	15	172	3	3	0	0	+	+	Obtained by tube; yellow, green slime	C
19	10	—	0	—	—	+	+	+	Obtained by tube; yellow, green slime	A
20	10	—	0	—	—	0	+	+	Obtained by tube; blood-stained mucus	A
21	10	17	1	0	1	+	+	+	Obtained by tube; thin, mucus and blood	A
22	10	—	0	—	—	0	0	+	Obtained by tube; thin mucus	A
23	10	—	0	—	—	0	0	+	Obtained by tube; thin, yellow feces	
24	18	57	5	5	0	0	+	+	Obtained by tube; green, muco-fecal	C
25	16	43	2	2	0	0	+	?	Obtained by tube; mucus	C
26	19	25	3	3	0	+	+	+	Obtained by tube; bloody mucus and feces	C
27	20	76	4	4	0	0	+	+	Obtained by tube; green mucus and feces	C
28	16	—	0	—	—	0	+	+	Obtained by tube; gray, with little mucus	C
29	18	—	0	—	—	0	0	+	Obtained by tube; thin, yellow feces	A
30	20	—	0	—	—	0	+	+	Obtained by tube; feces with little mucus	
31	12	—	0	—	—	0	+	+	Obtained by tube; feces with little mucus	
32	14	—	0	—	—	0	+	+	Obtained by tube; feces with green mucus	
33	18	—	0	—	—	0	+	+	Obtained by tube; green feces and curds with mucus	
34	18	—	0	—	—	0	+	+	Obtained by tube; green feces with mucus	
35	23	—	0	—	—	+	+	+	Obtained on pad; yellow feces, little mucus	
36	16	—	0	—	—	0	+	+	Obtained by tube; thick, yellow feces, little mucus	
37	18	—	0	—	—	0	+	+	Obtained by tube; thin, yellow feces and mucus	
38	18	—	0	—	—	0	+	+	Obtained by tube; thick, green feces, little mucus	
39	37	—	0	—	—	+	+	+	Obtained by tube; green feces with mucus	

A, examined by W. W. W. B, reported positive by Dr. Bassett, Wilson Sanitarium. C, examined by E. H. Shorer.

No. of Case.	No. Plates Made.	No. of Colonies Transplanted.	No. of Colonies of B. Dysenteriæ.	Type of Bacilli.		Blood in Stool.	Mucus in Stool.	Feces in Stool.	Description of Material Used.	Notes.
				"Harris."	"Shiga."					
40	36	—	0	—	—	0	+	+	Obtained by tube; green, thin feces with mucus	
41	18	70	2	0	2	—	—	—	Obtained on napkin; partly dried, blood-flecked stool	
42	16	60	5	5	0	+	+	+	Obtained by tube; small amt. feces and mucus	
43	18	87	1	1	0	+	+	+	Obtained by tube; green mucus	A
44	18	38	16	16	0	+	+	+	Obtained on napkin; green feces with mucus and blood flecks	
45	10	22	3	3	0	+	+	+	Obtained on napkin; thick mucus	
46	18	48	13	13	0	0	+	+	Obtained on napkin; green mucus	
47	24	325	1	1	0	+	+	+	Obtained on napkin; yellow feces with mucus and blood	

A, examined by W. W. W.

mucus in all cases but four, and blood was absent in 30 instances—hence in two-thirds of the cases studied.

If we consider only the instances (16 analyzed) in which the dysentery bacillus was found we find that blood occurred 8 times and mucus and feces in all. Of the 3 cases not included in the analysis in one the specimen was dried (case 4) and in two the bacillus was isolated later by Dr. Bassett at the Wilson Sanitarium.

REPORT OF ARTHUR I. KENDALL.

Boston.

From June 15th to September 15th, 1903, I was engaged under the auspices of the Rockefeller Institute for Medical Research in the investigation of the bacteriology of cases of diarrhea in children with especial reference to the occurrence of the bacillus of dysentery in the excreta. The children from whom I obtained specimens for examination were being cared for at the Boston Floating Hospital, although in this report there will be included three cases of infantile diarrhea which were investigated at the Infant's Hospital.

Before I take up the subject matter of this report I wish to express my great indebtedness for assistance and many courtesies to the following gentlemen without whose cordial cooperation this study would have been impossible: The Managers and Board of Directors, Drs. Hastings, Fennessey, Sturgis and Shay of the medical staff, Drs. Fairbanks and Breck of the visiting staff of the Boston Floating Hospital, Drs. Durgin and Hill of the Board of Health, who generously put at my use the facilities of the Bacteriological Laboratory of the Board, and Mr. Paul Lewis for his valuable aid in the latter part of the investigation.

In the course of the summer, stools from 35 children were studied—of these 35 cases of intestinal disturbance, 4 were due to causes which exclude them from consideration as a part of the study: thus two were cases of tuberculosis, one a case of typhoid fever and one of proctitis of transient character. Although they will not be considered further in this report they are of interest as examples of intestinal disease in which even very careful and often prolonged search failed to disclose the presence of the bacillus of dysentery.

The exclusion of these four extraneous examples of diarrheal disease reduces the number of cases investigated to 31, of which number 29 were found to yield cultures of Bacillus dysenteriae—a positive result in 93.5 per cent. With this introduction I will pass to a description of my methods and the details of the results yielded by them.

Culture Media.—For the plates I employed plain agar-agar made by Hill's method (Committee of the American Public Health Associa-

tion) in which the reaction was +5 instead of +15 as recommended by the committee. The reason for the change was the more luxuriant growth of the bacillus of dysentery upon a medium of that reaction. Indeed upon it the colonies of the dysentery bacillus grew often to a size of 2-3 mm. in 24 hours.

For the differentiation of the types of the bacillus, mannite-litmus-agar made also by Hill's method and containing 1 per cent agar-agar and deeply tinted with litmus was used. For the separation of the gas-producing from non-gas-producing colonies in the original transplantations I used throughout the greater part of the summer, glucose-agar, also prepared by Hill's method, but later, after Mr. Lewis' arrival and at his suggestion, I employed the semi-solid jelly of Hiss in which more rapid and certain gas-formation was detectable.

The other media including litmus-milk were prepared in the ordinary manner; the litmus-milk was sterilized by the discontinuous or fractional method in an Arnold's sterilizer.

Since the plates were poured at the Hospital and studied at the laboratory, which were separated by a considerable distance, the sterilized Petri dishes were carried in sterile copper boxes from and to the laboratory. In this way ordinary contaminations were entirely avoided.

Bacteriological Methods.—The plating of the specimens of dejecta was done immediately or quickly after the passage. At first, rather heavy suspensions were made and from them a second more dilute suspension was prepared by transferring 6 loops of the former to a second tube of bouillon. The plates were inoculated from this second mixture using 2-4-6-8 loops for the several tubes of agar-agar. As a rule eight plates were made from a single specimen this number being necessitated by the difficulty of transportation of the sterile dishes from the laboratory to the boat and back again to the laboratory. Later, one loop of the material was transferred to a tube of sterile water and this weak suspension then employed in seeding the plates. This latter method gave more uniform and satisfactory results.

After a given case was started, samples of the dejecta were plated at intervals of not more than four days, until the bacillus of dysentery was obtained in culture or had finally eluded detection in the rather large number of colonies among which it had been looked for. In my hands this procedure was more satisfactory than the alternative one of securing a larger number of plates from one sample of the discharges from the bowel. The plates were incubated at 37° C. in a moist incubator which I found to possess advantages over the dry oven.

Transplantation of colonies was begun after 18 hours of incubation. In about one-half of the plates the surface colonies remaining were now marked with the wax pencil and additional colonies of the "Shiga bacillus" appearance were removed in the same way at intervals of 24 hours until success attended the search. The bacillus of dysentery was, as a rule, recovered among the colonies transplanted at the first 24-hour period. In a few instances, however, it was obtained from the marked plates and not from the unmarked and hence at a later period. I am of the opinion that the early recovery of the bacillus at the end of 24 hours of incubation of the plates arose from the favorable character of the agar-agar medium as prepared by the Hill method since the growth upon it is strikingly luxuriant.

The final identification of the organisms supposed to be B. dysenteriæ was completed by means of a study of the morphology, the cultural characters upon the usual media, and the behavior towards anti-dysenteric horses' serum supplied by Dr. Flexner. The separation of the types now recognized—the "Flexner-Harris" and "Shiga"—was effected through the use of the litmus-mannite-agar.

The biological characters and cultural properties of the types of the bacillus of dysentery just mentioned are so well known or can be seen so readily in the publications of Vedder and Duval, Duval and Bassett and Gay and Duval, that they will not be described here. But I wish to draw attention to certain bacilli having certain close resemblances to B. dysenteriae, but which differ from that organism in their ultimate action upon the litmus-milk medium. What relationship, if any exists, is borne by these bacilli to the dysentery bacillus I am not able to state.

The typical dysentery bacilli cause no coagulation of milk, and at first produce a weak acidity, which reaction is brought back to amphoteric in about 72 hours, after which a mild and permanent alkalinity makes its appearance. I encountered two "varieties" of bacilli acting upon litmus-milk in the following manner:

a. The reaction becomes at first acid, then alkaline and finally and permanently, after about two weeks, acid.

b. The reaction becomes at first acid, then amphoteric and finally and permanently but slowly decidedly alkaline.

These "varieties" of bacilli agglutinate with the anti-dysenteric serum of the horse; they are, however, not included in the table as "dysentery bacilli." They were often associated in the intestinal contents with the typical organisms.

In two instances I met with what at first appeared to be a para-

doxical result in the cultures. Organisms were obtained from the plates, which gave all the reactions of B. dysenteriae, but upon subsequent investigation, some 5 weeks later, gas production in glucose media was found to be produced by them. The explanation of this anomalous behavior of the dysentery bacilli was ascertained by plating the suspicious cultures, when a small number of colon bacilli were discovered to be mingled with the former organisms. I mention this experience in order to point the moral that, in attempting isolation of intestinal bacteria directly from the discharges, colony appearance is not necessarily the equivalent of purity, and hence equivocal and confusing results of subcultures may easily be the result of admixtures and not necessarily due to "variations" in the prevailing form of microorganism.

Concerning the number of dysentery bacilli in the discharges, my experience does not permit me to hazard a statement. If the number of bacilli recoverable from the plates be taken as an index of relative proportion, then they must be regarded as in the great minority as compared with the other intestinal bacteria which grow upon the plates. When, however, we stop to consider how every improvement in the culture medium, so far as this organism is concerned, tends to increase the ease of its isolation, we may well inquire whether our present methods of recovery give us an adequate idea of the real richness of the specimens in dysentery bacilli. In only one case (No. 16) of my series did the number of dysentery bacilli appear to be large and in this it was considerably below the number of colonies of non-dysenteric bacilli which grew upon the plates.

I regret that the pressure of work prevented me from making a study of the agglutinating properties of the blood of the children from whom the dysentery bacilli were obtained. This test was made in a few instances but as it could not be carried out regularly I did not pursue it as I had hoped to do. I was impressed by Dr. Flexner with the desirability of studying with thoroughness the distribution of dysentery bacilli in the discharges of children suffering from diarrhea and hence I sacrificed all other features of the investigation to this one. Moreover, it would have been easy, in view of the large number of cases which came for treatment to the Floating Hospital, to have considerably enlarged the total number of cases examined. But here again I readily coincided with his view that thoroughness of investigation of individual cases was more important than a less exhaustive study of a larger number of children.

Since my study has been so uniform, it is worth while to inquire

No. of Case.	Number of Plates Made.	Colonies of B. Dysenteriæ.	Type of Bacilli.		Blood in Stool.	Mucus in Stool.	Feces in Stool.	Description of Stool.	Notes.
			"Harris."	"Shiga."					
1	16	+	o	+	+	+	o	Green-yellow, fluid; blood flecks	
2	10	+	o	+	o	+	+	Green-yellow, fluid	
3	10	+	o	+	o	+	+	Green-yellow formed	
4	16	+	+	o	o	+	+	Green-yellow; mod. mucus	
5	28	+	+	o	o	+	+	Formed with little mucus	Dysentery bacilli scarce.
6	10	+	+	o	o	+	o	Yellow-green mucus	
7	20	+	+	o	o	+	+	Green-yellow; mod. mucus	
8	35	+	+	o	—	—	—	Scraping from intestine post mortem.	Dysentery bacilli scarce.
9	7	+	+	o	o	+	+	Green-yellow; much mucus	
10	32	+	+	o	+	+	+	Bloody mucus and feces	
11	10	+	+	o	o	+	+	Yellow-green; mod. mucus	
12	18	+	+	o	o	+	+	Yellow-green; little mucus	
13	12	+	+	o	o	+	+	Yellow-green; little mucus	
14	16	+	+	o	o	+	+	Yellow-green; mod. mucus	
15	16	+	+	o	+	+	o	Blood and mucus	
16	8	+	+	o	+	+	o	Blood and mucus	Large number of dysentery bacilli present.
17	26	o	—	—	o	+	+	Cultures from intestinal contents post mortem.	Tuberculous ileocolitis.
18	16	+	+	o	o	+	+	Yellow-green; mod. mucus	
19	19	+	+	o	o	+	+	Yellow-green; mod. mucus	Proctitis.
20	8	o	—	—	+	+	o	Blood and mucus	
21	32	+	+	o	o	+	+	Yellow-green; mod. mucus	Dysentery bacilli scarce.
22	56	o	—	—	+	+	+	Variable	Typhoid fever. Many typhoid bacilli isolated. Blood positive to Widal test.
23	9	+	+	o	o	+	+	Yellow-green; mod. mucus	
24	16	+	+	o	o	+	+	Yellow-green, formed; mod. mucus	
25	14	+	+	o	o	+	+	Greenish fluid; much mucus	
26	32	+	+	o	o	+	+	Green-yellow, formed ; little mucus	Bacilli bleached nally milk.
27	7	+	+	o	o	+	+	Solid, brownish-black; much mucus	
28	35	+	+	o	o	+	+	Green-yellow, semi-fluid; mod. mucus	Dysentery bacilli scarce.
29	8	+	+	o	o	+	+	Green-yellow, semi-fluid; mod. mucus	
30	9	+	+	o	o	+	+	Green-yellow, semi-fluid; much mucus	
31	16	+	+	o	o	+	+	Green-yellow, semi-fluid; mod. mucus	
32	40	o	—	—	o	+	+	Green-yellow, semi-solid; mod. mucus	
33	16	o	—	—	o	+	+	Green-yellow, semi-fluid; mod. mucus	Tuberculosis.
34	17	+	o	+	o	+	+	Green-yellow, semi-solid; mod. mucus	
35	34	o	—	—	o	+	+	Green-yellow, semi-solid; mod. mucus	

whether the precise character of the discharges greatly influenced the results. If the table is scrutinized it will be observed that the number of plates used in the investigation of the different cases varied greatly, and, if it is recalled that the cases were studied in series of 8 plates per examination, some notion can be obtained of the relative ease or difficulty with which a positive result was achieved. This test is of course not absolute, and much may have depended on accidental circumstances, but taken altogether it probably is the most reliable one at our disposal to establish the variation in occurrence of the bacilli.

The smallest number of plates studied in single instances were in connection with cases 2, 3, 6, 9, 11, 16, 20, 23, 27, 29, 30 in which from 7 to 10 plates were used. Eliminating case 20 which was negative, we have 10 cases yielding the bacilli with relative ease. Of these cases, blood was present in quantities visible to the naked eye in one case only; mucus was present in all cases, and feces in all but two cases. On the other hand, case 16 of this series in which blood occurred yielded the largest number of dysentery bacilli of all the specimens examined.

The constant abnormal constituent of the stools was mucus, the quantity and appearance of which were subject to great variations. Of the 35 cases investigated, which represent the entire number of children ill of all diseases, the discharges in all contained mucus, while in only 6 was blood discovered. A microscopical study of the dejecta with a view of determining the occurrence of extravasations of small numbers of red corpuscles was not made.

REPORT OF PAUL A. LEWIS, STUD. MED.,

Philadelphia.

The cases studied in Philadelphia occurred in parts of the city widely removed from one another. The central point from which materials were to be drawn was the Children's Hospital, but at the critical moment—during the height of the hot season—the hospital was closed during a period of three weeks on account of an epidemic of diphtheria. I was therefore obliged to depend for material for study upon hastily formed associations with other institutions. Later on in the season the Children's Hospital reopened and during July and August a number of specimens was obtained from that source. My work in Philadelphia was, however, interrupted and finally brought to an abrupt close through my transfer first to New York and then to Boston to assist in the investigations which were being conducted in those places. Therefore, the number of cases of diarrheal disease in children investigated bacteriologically in Philadelphia is smaller than it would have been but for the interruptions mentioned. Perhaps the total results, too, are different from what they might have been had opportunity been afforded to follow more carefully some of the negative cases.

I am indebted for the material for my study to the following physicians to whom I wish to express my appreciation of many kindnesses shown me: Drs. Hand and Wieher, of the Children's Hospital; Dr. Hamill, of the Polyclinic Hospital; Drs. Griffiths, Ostheimer and Levy, of the University Hospital, and Dr. Newmayer through whom the cases in the tenement district came into my hands.

I am enabled through the courtesy of the physicians in charge of the cases to include brief clinical descriptions and diagnoses of the cases examined.

METHOD OF WORK.

Collection of Stools.—The stools were taken on the ordinary napkins. Every effort was made to get the discharges as soon after they were passed as possible. However, in the earlier half of the summer—cases 1 to 15—this point was not so rigidly insisted on. If an hour

Case.	Diagnosis and Description.	Bacteriological Result. +=Pos. —=Neg.
1	Acute ileo-colitis: severe ; sudden onset with fever. Slow recovery.	+Early
2	Summer diarrhea : chronic case with periodic exacerbations of severe symptoms ; onset in late winter; patient poorly nourished and debilitated.	+
3	Summer diarrhea: child slightly ill ; no careful examination could be made	—
4	Acute ileo-colitis with pneumonia : marked toxic symptoms. Death end of first week ; autopsy.	+
5	Acute ileo-colitis with pneumonia: death shortly after admission ; autopsy ; mild intestinal lesions.	—
6	Summer diarrhea—moderately severe and persistent: no fever, little prostration	+
7	Gastro-enteritis: moderately severe, later became chronic and fatal termination expected.	+
8	Acute ileo-colitis: case with relapses and severe intestinal symptoms.	+
9	Gastro-enteritis: severe diarrhea; slight constitutional symptoms and quick recovery.	+
10	Ileo-colitis with pneumonia: not followed.	—
11	Gastro-enteritis: chronic case with severe diarrhea.	—
12	Gastro-enteritis: early history, suspected intussusception; late relapses; chronic course. Autopsy: pseudo-membranous ileo-colitis.	+
13	Ileo-colitis: not followed.	—
14	Ileo-colitis: chronic case—not followed.	—
15	No history.	—
16	Acute ileo-colitis: severe case with fever and prostration; relapse.	+
17	Ileo-colitis: bloody and mucous diarrhea without prostration or fever; not followed.	—
18	Ileo-colitis: no history.	+
19	Ileo-colitis with pneumonia: autopsy showed mild intestinal lesions and extensive pulmonary consolidation.	+
20	Ileo-colitis: chronic case; not followed.	—
21	Ileo-colitis: chronic case; not followed.	—

or two had elapsed before the specimen was obtained it was still used providing no later one was available. During the remainder of the summer no stool was taken which had not been passed within the hour

and great effort was made to obtain them within a few minutes of the time of passage. At first the napkins were carried to the laboratory and suspensions were made there. Later, tubes of culture medium and an alcohol lamp were taken and suspensions made on the spot. The table which follows shows the time elapsing between the passage of the stools and the plating:

POSITIVE CASES.			NEGATIVE CASES.		
Number.	Elapsed Time.		Number.	Elapsed Time.	
	Hours.	Minutes.		Hours.	Minutes.
1	..	30	3	3	..
2	2	..	5	4	..
4	5	..	10	4	30
6	3	30	11	2	..
7	1	30	13	2	..
8	4	..	14	4	..
9	2	..	15	4	..
12	1	30	17	4	..
16	1	..	18	1	..
19	1	15	21	2	15
20	1	15			
Maximum	5	..	Maximum	4	..
Minimum	..	30	Minimum	1	..
Average	2	4	Average	3	4

Plating.—From the stool when obtained I made suspensions in salt solution or bouillon. The mucus, as free from fecal matter as possible, was transferred to the tubes. When blood was present it also was admitted to the suspension but in none of these cases was it possible to plate blood alone distinct from the mucus. At first enough mucus was transferred (3—5 loops) to make a cloudy suspension after shaking. From this first tube 6 loops were put into a second suspension and from this tube all the plates were made. The seeding was varied by changing the number of loops transferred to the agar tubes. The best plates, as a rule, were those which contained 3—4 loops of the second suspension. Later in the summer, the first suspension was made so light that when it had settled after a vigorous shaking the supernatant fluid was not clouded. Then 1—2 loops were transferred to the agar tubes. The difficulty was to get the right amount of material suspended, the plates at first being always too thickly seeded. In several cases I tried washing the mucus through one or two tubes of sterile water to free it from all fecal matter. In the first case tried in this way a surprisingly larger number of colonies of the dysentery bacillus developed in the plates. I had formed great hopes

upon this variation and introduced it into the later work, but I did not find it to yield results which were better than those given by the first method employed.

The plating medium was 1.5 per cent. agar-agar made with beef extract and kept slightly but distinctly acid to litmus.

Marking and Picking Colonies.—I followed the Vedder-Duval method of incubating the plates and marking the superficial colonies after 12—24 hours incubation. In the early summer I always returned the marked plates to the thermostat, but later, after my fifth case, I made it a rule to pick about 30 colonies of the first crop. On the basis of my summer's work I can form no satisfactory estimate of the relative advantages of the two procedures; but I can affirm the possibility of securing colonies of B. dysenteriae among the results of this first transplantation.

The great variation in number of dysentery colonies recoverable from the plates makes any rule as to the extent of the picking to be followed unreliable. In no case reported as negative were less than 150 colonies transferred; in one case 500 colonies were tested with negative results. The positive cases were yielded more readily. From the plates of Case VIII. I picked in all 35 colonies, of which 28 proved to be B. dysenteriæ. I have, however, in one instance, taken off 200 colonies to secure in the end a single tube of the dysentery bacillus.

Transplanting Media.—At the beginning of the summer, glucose agar was used as the medium to separate gas-producers from the non-gas-producers in glucose-containing media. This medium will show gas formation in 12—24 hours as a rule; sometimes, however, it is delayed for 48 hours. The litmus mannite-agar can also be used for this purpose and acts more quickly and unequivocally, in my opinion, besides which it serves the purpose of giving a primary differentiation of the two types of dysentery bacilli when present. But the difficulty of preparing the medium, where such large quantities are to be used, is a drawback. After my return from New York where I had spent 10 days with Duval I employed exclusively the semi-solid jelly of Hiss. I found this medium not only to show gas production quickly, but also to indicate motility and to bring out a fairly characteristic form of growth of B. dysenteriae.

Subsequent Procedures.—Having adopted the Hiss medium as recommended by Duval I also followed his method for the demonstration of the identity of the bacillus of dysentery by studying directly from this medium the morphology and agglutinative properties of suspected organisms. Next, the organisms were transferred to the

litmus-milk and litmus mannite-agar media. From this point on, the identification of the organism and differentiation of types offer no difficulties. I followed the usual methods pursued, paying strict attention to the changes occurring in the milk medium.

RESULTS OF THE STUDY.

Of the 21 cases examined, 11 yielded positive and 10 negative bacteriological results so far as the bacillus of dysentery was concerned—in other words, the organism was isolated from stools in 52.5 per cent. of the cases.

Case Number.	Number of Plates Made.	Number of Colonies of B. dysenteriæ isolated.	Type of Bacilli.		Blood in Stool.	Mucus in Stool.	Feces in Stool.	Agglutination of Blood.	Brief Description of Stool Examined.	Source of Material.
			"Harris."	"Shiga."						
1	12	2	2	0	+	+	0	1.40	S. Blood-flecked mucus	U. H.
2	29	11	0	11	+	+	+	——	S. Large, curdy; fecal, with mucus and blood flecks	T. D.
3	18	0	—	—	+	+	+	——	S. Formed fecal with little mucus but much blood	T. D.
4	8	2	2	0	+	+	0	——	S. Mucus flecked with blood	P. H.
5	18	0	—	—	0	+	+	——	S. Large, cheesy and fecal; little mucus	C. H.
6	21	16	16	0	0	+	+	——	S. Undigested food with mucus	T. D.
7	18	14	0	14	0	+	+	——	S. Some feces with much mucus	C. H.
8	30	28	28	0	+	+	+	——	S. Scanty; bloody mucus with feces	T. D.
9	26	9	9	0	0	+	+	——	S. Large; muco-fecal	T. D.
10	28	0	—	—	0	+	+	——	S. Curds and feces; little mucus	C. H.
11	27	0	—	—	0	+	+	——	S. Much feces, little mucus	C. H.
12	15	1	1	0	0	+	+	——	S. Scanty; mucus and feces	C. H.
13	30	0	—	—	0	+	+	——	S. Scanty; green mucus with feces	C. H.
14	30	0	—	—	0	+	+	——	S. Curds and mucus	C. H.
15	20	0	—	—	0	+	+	——	S. Curds and little mucus	R.B.S
16	21	1	1	0	0	+	+	——	S. Scanty; muco-fecal	U. H.
17	18	0	—	—	+	+	+	——	S. Large; mucous and fecal; blood streaks	T. D.
18	23	7	7	—	+	+	+	——	S. Muco-fecal with blood flecks	C. H.
19	24	10	0	10	0	+	+	1:100	S. Large; muco-fecal	C. H.
20	28	0	—	—	0	+	+	——	S. Curds, mucus and feces	C. H.
21	27	0	—	—	0	+	+	——	S. Large; muco-fecal	C. H.

U. H.=University Hospital. T. D.=Tenement district. P. H.=Polyclinic Hospital. C. H.=Children's Hospital. R. B. S.=Red Bank Sanitarium.

As to types, the bacillus which I recovered was in 8 cases the "Flexner-Harris" and in 3 cases the "Shiga" organism. In no case were both types of bacilli found associated.

The agglutination reactions of the bacilli isolated and identified as the bacilli of dysentery were tried with anti-dysenteric serum from the horse. These reactions were positive, although in the case of certain

bacilli, subcultivations were needed to bring out a good reaction. The best results were obtained through the use of serum having an origin agreeing with the type of the bacillus, but cross-agglutinations were also obtainable. Very few tests were made with the blood of patients, as it was found very difficult to secure, under the conditions in which I worked, sufficient blood for accurate examination.

In conclusion, I should like to state that as I look back upon my results through the experience I gained later in the summer in New York, with Duval, and in Boston, with Kendall, I am inclined to consider that many of the cases reported by me as negative were in reality examples of dysentery bacillus infection, and that better conditions of work and doubtless also more experience on my part, would have caused many of them to yield a part of their content of the bacillus of dysentery.

REPORT OF V. H. BASSETT, M.D.,

Baltimore.

The entire number of cases studied was 73, in 51, of which or 70 per cent., the dysentery bacillus was found. The materials employed in the 51 positive cases consisted of the discharges from the intestine in 44 and mucus, etc., obtained directly from the bowel in 7 instances.

The discharges contained invariably mucus, although the amount was subject to great variation. The table gives an approximate estimate of the quantity present in each instance. Blood was less frequently present, being noted in 24 cases. In other words, in nearly one-half of the examples of infection with B. dysenteriæ, blood in quantities visible to the naked eye was absent. In quantity the blood also varied considerably and oftenest occurred in the form of points and small streaks—so-called flecks. Feces were noted 12—14 times as forming a portion of the material used for the cultivation of the bacillus.

The number of colonies of the dysentery bacillus taken off the plates varied within wide limits. In a few instances one or two colonies only were obtained, and the majority of the cases yielded small numbers of colonies. Just what interpretation is to be placed upon this

[Editor's Note: Dr. Bassett's studies were carried out at the Wilson Sanitarium near Baltimore and extended through the summer months of 1903. The report supplied by Dr. Bassett consists of the records of the cases studied and a letter in which these are briefly reviewed. The following report, which I have constructed upon the basis of the records and letter, would seem to cover all the points which are essential; but I am sure that had Dr. Bassett written the report he would have presented features of interest which through ignorance I cannot do. At this distance (Germany) and in view of the brief time at my disposal for completing the series of reports on the summer's work, I am unable to communicate with Dr. Bassett so as to secure a personal report which should be ready for immediate publication. Fortunately his records are minute and full so that no doubt exists as to their significance. I find myself regretting, however, one omission that I wish might be supplied, namely, a statement of the method pursued by him for isolating the bacillus of dysentery. Since he says nothing about this matter I am led to suppose that he has not departed in the main from the method employed by him and Duval, the previous summer, which is essentially that used by Vedder and Duval. Mention is, however, made that the discharges were collected upon sterile gauze pads.—Simon Flexner.]

fact is not evident. That the materials used for the plating play an important part will later become clear, and it seems highly probable that the best method at present at our disposal for isolating the bacillus leaves much to be desired.

The absence of relationship between the number of plates poured and the number of colonies of B. dysenteriæ recovered is easily accounted for. The entire series of plates, even when this is small, may not be gone through minutely. If success attends the early picking of colonies no further use is made of the plates, and it is only in the cases in which difficulty of isolation is experienced that the full number of plates is closely studied.

There is undoubtedly a fluctuation from time to time in the number of dysentery organisms thrown off with the discharges or recoverable in them. In nine cases (4, 5, 9, 10, 26, 27, 45, 47, 48) more than a single examination was made and in one instance only in each case, was the dysentery bacillus secured. In at least one instance (Case 8) the number of bacilli present, at the time of successful cultivation, appears to have been quite considerable, and in another (27) after a successful cultivation from a stool, a subsequent scraping from the rectum after death gave negative results.

On the other hand, the second and third trials may exceed the first in the number of colonies recovered. In all, 19 cases were studied more than once with positive results. I will give a few illustrative examples:—Case 12: 1st plating, 5 colonies; 2d plating, 16 colonies; 3d plating, 8 colonies; 4th plating, 10 colonies. Case 38: 1st plating, 9; 2d, 26 (these two plated on same day using separate stools); 3d, 3 colonies. Case 39: 1st plating, 48; 2d, 3; 3d, 20; 4th, 6 colonies, all on the same day from different stools. The importance of repeated examination in inconclusive cases as well as the bearing of the fluctuation-factor is well brought out by these figures.

In several cases in which the stools were negative the examination of material derived directly from the intestine gave the bacillus of dysentery. Thus stools from Case 9 were examined on June 26th and 30th without yielding the bacilli; while a scraping from the rectum taken on July 4th yielded two colonies of the organism. Case 20, having failed to yield the bacillus from a stool and from mucus obtained through the passage of a rectal tube, a scraping from the mucosa at autopsy gave a positive result. Case 21 had been examined twice negatively (stools) and once positively (rectal scraping) during life. At the autopsy, cultures were obtained from the mucosa of the colon and an ulcerated Peyer's patch.

That the bacillus of dysentery is more readily recovered from the mucosa of the intestine than from the discharges follows from what has been stated upon that subject; but the fact is also proven by the rare failures that follow the employment in cultures of portions of the mucous membrane or the mucus derived immediately from the pathological tissue. We were almost uniformly successful in obtaining the dysentery bacilli from all the cases that came to autopsy and from a number in which rectal scrapings were carried out during life in which the stools had failed to yield the organism. In one case only (*27*) did a post mortem rectal scraping give negative results although in two additional cases (2 and 13) in which the material was obtained directly from the bowel during life, failures were recorded. In 7 autopsies the bacilli were recovered from the intestines. In one instance, case 14, the bacilli were obtained from a stool on August 19th, whereas they were missed in the post mortem scraping taken 3 days later. In the latter set of plates innumerable streptococci developed.

The bacillus of dysentery and streptococci in large numbers may exist side by side on the plates without preventing each other's development. Thus we noted the association of streptococci in small or moderate numbers with the dysentery bacillus in many cases, and in very large numbers in 14 cases from which the bacillus was secured. While this association may be of considerable clinical significance, it is not opposed to the isolation of the bacillus of dysentery in cultures.

Case 51 yielded a good number of colonies of B. dysenteriae, but is interesting chiefly as bringing out the contagious nature of the diarrhea from which the child suffered. In the family to which this child belonged three cases of diarrhea developed. The first case occurred sporadically and then, after an interval of a few weeks, a second, and 10 days later, a third case appeared.

Some attention was paid to the reaction of agglutination, the blood of the sick children being used in making the tests. Agglutinations were the rule in cases in which the bacilli were present (see table) and in degree they not uncommonly reached a dilution of 1 :1000 to 1 :1500. Still there were notable exceptions to this rule for which no explanation is at hand. The cases which gave negative results in the bacteriological study yielded far fewer positive reactions of agglutination. Since it is possible in a given instance to fail to secure the dysentery bacillus from an otherwise suspicious case of diarrhea, I am disposed to regard a high agglutination as indicating infection with that bacillus. Unfortunately the contrary is not true, for absence of the reaction does not exclude either the infection or failure to recover the specific bacillus.

POSITIVE CASES.

Case Number.	Number of Plates Made.	Number of Colonies of B. dysenteriæ.	Type of Colonies. "Harris."	Type of Colonies. "Shiga."	Blood in Stool.	Mucus in Stool.	Feces in Stool.	Description of Material Used for Cultures. S.=Stool.	Agglutination of Blood. Positive.	Agglutination of Blood. Negative.	Day of Disease Blood Tested.	Termination.
1	12	3	3	0	—	—	—	Scraping from colon post mortem.	1:1,000		28	Death.
2	12	3	3	0	0	+	+	S. Yellow; muco-fecal	1:20		17	Not stated.
3	12	4	4	0	0	+	+	S. Muco-fecal	1:100		9	Death.
4	8	3	3	0	0	+	0	S. Scanty, green; muco-purulent.	1:1,000		17	Not stated.
5	8	3	3	0	0	+	+	S. Muco-fecal; mod. mucus	1:1,000		16	Not stated.
6	12	15	15	0	+	+	0	S. Scanty, muco-pur., with flecks of blood		1:20	22	Not stated.
7	24	3	3	0	0	+	+	S. Mucus with much feces	1:100		16	Not stated.
8	11	25	25	0	+	+	+	S. Large, muco-fecal with blood				Not stated.
9	12	2	2	0	—	—	—	Rectal scraping during life	1:50		9	Not stated.
10	20	4	4	0	+	+	+	S. Yellow muco-pur.; blood microscopical				Not stated.
11	20	4	4	0	+	+	0	S. Scant; green mucus; flecks of blood		1:20	20	Not stated.
12	6	5	5	0	+	+	0	S. Muco-pur., with blood flecks		1:20	33	Not stated.
13	14	4	4	0	0	+	0	S. Curdy; mucus and pus				Not stated.
14	8	8	8	0	+	+	0	S. Muco-pur., bloody	1:1,500		?	Death.
15	12	2	2	0	+	+	0	S. Much mucus; blood flecked				Not stated.
16	12	14	14	0	+	+	0	S. Muco-pur.; with blood flecks				Not stated.
17	16	30	30	0	0	+	0	S. Muco-purulent				Not stated.
18	12	7	7	0	—	—	—	Rectal scraping during life		1:20	4	Not stated.
19	12	5	5	0	0	+	+	S. Large; muco-fecal	1:50		20	Not stated.
20	6	47	47	0	—	—	—	Scrapings from colon p.m.		1:20		Death.
21	12	10	10	0	—	—	—	Rectal scraping during life	1:1,000		?	
22	12	36	36	0	+	+	0	S. Green; blood-stained muco-pus				Not stated.
23	12	23	23	0	+	+	0	S. Bright red; bloody mucus	1:1,000		?	Not stated.
24	12	2	2	0	0	+	0	S. Scant, green; mucus	1:100		?	Not stated.
25 *	12	1	1	0	+	+	0	S. Fluid, muco-pur.; blood flecks	1:100		?	Not stated.
26	8	2	2	0	0	+	0	S. Muco-purulent	1:500		?	Not stated.
27	18	3	3	0	0	+	0	S. Watery, greenish mucus	1:1,000		3	
28	24	5	5	0	0	+	+	S. Abundant green mucus, yellow feces	1:100		?	
29	10	8	8	0	+	+	0	S. Green mucus with little blood	1:1,000		3	
30	18	10	10	0	+	+	0	S. Green; muco-pus with little blood		1:20	?	

* Larger number of organisms secured at other platings.

POSITIVE CASES. (Continued.)

Case Number.	Number of Plates Made.	Number of Colonies of B. dysenteriæ.	Type of Colonies. "Harris."	Type of Colonies. "Shiga."	Blood in Stool.	Mucus in Stool.	Feces in Stool.	Description of Material Used for Cultures. S.=Stool.	Agglutination of Blood. Positive.	Agglutination of Blood. Negative.	Day of Disease Blood Tested.	Termination.
31	11	10	10	0	—	—	—	Rectal scraping during life	1:100		?	
32	18	2	2	0	+	+	0	S. Small mucus blood stained	1:100		?	
33	18	3	3	0	+	+	+	S. Fecal with bloody mucus		1:100	?	
34	15	2	2	0	+	+	0	S. Scanty; muco-pus and blood		1:20	?	
35	15	9	9	0	+	+	0	S. Mucus with blood staining				
36	6	2	2	0	+	+	0	S. Mucus and blood				
37	24	3	3	0	—	—	—	Rectal scraping during life	1:1,000		?	
38	12	9	9	0	+	+	0	S. Mucus and blood	1:100		?	
39	12	48	48	0	+	+	0	S. Blood-stained muco-pus		1:50	?	
40	7	7	7	0	0	+	0	S. Mucus	1:100		?	
41	24	6	6	0	0	+	0	S. Mucus and curds				
42	9	8	8	0	+	+	+	S. Curds, feces, muco-pus, blood	1:1,000		?	
43	12	81	81	0	+	+	?	S. Scanty; green muco-pus and curds	1:1,000		?	
44	24	3	3	0	0	+	0	S. Small mucus	1:1,000		?	
45	24	4	4	0	0	+	0	S. Small mucus	1:250		?	
46	—	4	4	0	0	+	0	S. Scanty; muco-pur.	1:100		?	
47	24	3	3	0	0	+	+	S. Small mucus and fecal		1:50	?	
48	24	4	4	0	0	+	?	S. Green mucus and curds	1:200		?	
49	15	5	5	0	+	+	0	S. Muco-pus and blood				
50	12	10	10	0	0	+	+	S. Mucus and feces	1:250		?	
51	12	20	20	0	+	+	0	S. Muco-pus and blood	1:200		?	

As regards the duration of the reaction I would record merely the two instances (50, 51) in which the blood was still active three months after recovery from diarrheal disease.

(Bassett writes of the cases in which he failed to isolate the dysentery bacillus: "Of the negative cases many were undoubtedly examples of infection with the dysentery bacillus. In some the organism was missed either because of simple failure to recover it or by reason of failure to follow the cases promptly in the rush of work which came about the 18th of July. After arrangements were made which insured a steady supply of culture media I missed few cases. On the other hand, the negative group includes a number of examples which I think were clearly not infections with the bacillus of dysentery; these

NEGATIVE CASES.

Case number.	Number of Plates Made.	Blood in Stool.	Mucus in Stool.	Feces in Stool.	Description of Material Used for Cultures. S.=Stool.	Agglutination of Blood. Positive.	Agglutination of Blood. Negative.	Day of Disease Blood Tested.	Notes.
1	12	o	+	+	S. Scanty mucus and fecal	1:50		17	Plates not marked and only eight colonies subcultured
2	12	—	—	—	Rectal scraping during life		1:50	17	Examined during convalescence.
3	12	o	+	+	S. Fluid, fecal with green mucus and pus		1:50	?	Plates poorly seeded.
4	8	o	+	+	S. Green mucus and white muco-pus		1:50	15	Second test plates heavily seeded and failure. Streptococci numerous.
5	—	o	+	+	S. Much brown fluid feces with mucus		1:50	?	
6	8	o	+	+	S. Green curds, feces and mucus		1:50	26	Two sets of plates made.
7	4	o	+	o	S. Scanty mucus		1:20	24	One specimen only secured.
8	12	o	+	o	S. Green muco-pus		1:50	24	
9	8	o	+	o	S. Abundant green mucus	1:1,000		29	Few subcultures from plates made.
10	12	o	+	o	S. Muco-pus and curds		1:50	29	Few subcultures from plates made.
11	12	+	+	o	S. Muco-pus and blood-flecks	1:1,000		8	Few subcultures from plates made. Second specimen could not be obtained.
12	12	o	+	o	S. Muco-purulent				Plates overgrown with B. proteus. Second specimen not obtained.
13	12	—	—	—	Rectal scraping during life		1:50	18	Stool also negative.
14	10	o	+	+	S. Yellow, fluid; muco-pus and feces		1:50	?	
15	10	o	+	+	S. Fecal with little mucus	1:500			Streptococci numerous.
16	12	o	+	?	S. Small, pasty muco-purulent				
17	12	o	+	+	S. Fluid, yellow with green mucus				Second plates also negative.
18	6	o	+	o	S. Green mucus				
19	12	o	+	o	S. Small, green mucus		+	?	Numerous streptococci
20	12	o	+	+	S. Fecal with mucus				Second plates also negative.
21	24	o	+	o	S. Small, green mucus	1:1,000			Two other stools negative.
22	15	o	+	o	S. Small, green mucus				Second plates also negative.

were cases of mucous diarrhea of other origin." As regards the streptococcus Bassett states: "I am also convinced that the streptococcus is concerned in, and is at least a cause of secondary infection.")

THE PATHOLOGICAL ANATOMY OF SHIGA BACILLUS INFECTION OF THE INTESTINE IN INFANTS.

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(From the Laboratory of the Babies' Hospital, Oct., 1903.)

The *Bacillus dysenteriæ* (Shiga), first proved by Shiga[1] to be the cause of the epidemic dysentery of Japan, has been shown by the work of Flexner, Kruse, Müller, Deycke and others to stand in direct causal relation to the dysenteries, epidemic, endemic and sporadic, of the tropical and temperate zones, and its etiological importance is now universally recognized.

The pathological lesions in adults induced by infection with this bacillus were briefly stated by Shiga[2] to be more superficial than those caused by the amœba coli, and he noticed that while the mesenteric glands were regularly enlarged the spleen, unless some complication was present, was unaffected.

Flexner[3] reports briefly the autopsies of three cases in Manila, the lesions consisting in swelling, congestion and slight hemorrhage into the mucous membrane, with slight exudation on the surface in one case and very small ulcerations in another. He states that histologically "the changes appear in the mucous membrane, submucosa and muscularis, being most marked in the former situations. Those of the mucous membrane consist of coagulative necrosis, with exudation of fibrin and polymorphonuclear cells. . . The pseudo-membrane is a close-meshed network of fibrin enclosing multinuclear, often fragmented cells. . . . The submucosa is always much altered. . . . Here are found hemorrhages of variable size, while in the interstices of the tissue some fibrin appears. More marked, however, are cellular accumulations which are present, not uniformly, but in irregular areas. . . . The character of the cellular exudate is quite uniform. Excluding the red blood cells, the new cells consist chiefly of plasma cells. . . . In the submucosa, infiltration, hemorrhage and fibrin formation take place also beneath an intact or almost intact mucous

membrane. . . . The muscular coat shows only hemorrhages. . . . The peritoneal tunic is usually unaltered."

He emphasizes the fact that the polymorphonuclear leucocytes play a very insignificant rôle in the process of infiltration in the submucosa, whereas in the affected mucous membrane they are much in evidence. The bacteria were abundant in the fibrinous exudation on the mucous membrane and in the necrotic tissue; he could not find them in the unaffected tissue and believed the changes in the submucosa to be toxic in origin.

Strong and Musgrave[4] gave a summary of the changes observed in many autospies performed by them in Manila. They found the changes mostly in the large intestine but extending usually for a variable distance into the ileum. The whole wall of the intestine was thickened. The superficial part of the mucosa was necrotic and usually hemorrhages were found beneath this. The solitary follicles were swollen and red. In the very acute cases no definite ulceration was observed, but only a general superficial necrosis of the mucosa. Microscopically there was necrosis of the mucous membrane, with distention of the blood vessels and extravasation of blood. An extensive cellular infiltration of the mucosa was the rule, and there were hemorrhages into the submucosa and edema of the same. Plasma cells were increased, especially around the blood vessels. Edema was found even in the muscular coats. The mesenteric glands were uniformly much enlarged. Bacilli of typhoid-colon form and staining properties were found in the mucosa, and cocci often mixed with them, and though the latter were only superficially situated the bacilli were found sometimes not only in the mucosa but all through the areolar tissue, the muscularis mucosæ and submucosa down to the muscular coats. In the other organs were no constant changes. No mention is made of fibrin.

Duval and Bassett[5] in a preliminary paper first pointed out the relationship between the *B. dysenteriæ* (Shiga) and the summer diarrheas of infants. They studied forty-two positive cases.

Wollstein[6] reports the finding of the bacilli in thirty-nine cases of infantile diarrhea during the winter months, out of one hundred and fourteen studied, but many of the negative cases were in normal children and in all cases having blood and mucus in the stools the bacilli were present.

Numerous other cases in addition have been reported and the *B. dysenteriæ* (Shiga) is now generally accepted as the cause of the majority of the various forms of diarrhea in children.

The apparent discrepancies in the different types of cultures ob-

tained from various sources have partly disappeared in the light of the observations of Martini[7] and Lenz[8], who showed by reactions and cultural characteristics that there are at least two types of this organism, known to us as the true Shiga, not fermenting mannite, and the "Flexner-Harris," fermenting mannite. The latter of these is the type chiefly found connected with infantile diarrhea in New York, according to Wollstein, only one of her positive cases being of the true Shiga type.

Gay and Duval[9] have recently reported three cases in adults in which both types of the organism were found, in one case the acid-producing or "Flexner-Harris" type predominating, in another the alkaline or true Shiga type, and in a third the number of positive tubes were approximately the same. No cases of double infection in infants have as yet been found.*

The autopsies whose findings I wish to report took place at the New York Foundling Hospital, the Babies' Hospital and the Nursery and Child's Hospital.

The organism was proved to be present in the great majority of cases by an examination of the stools, but in seven cases it was obtained post-mortem by scraping the mucous membrane of the colon, and in three cases it was obtained both ante-mortem and post-mortem.

The organism found in these cases corresponded in all particulars to the type known as the acid-producing or "Flexner-Harris" organism; that is, it did not ferment glucose, saccharose or lactose, but did split mannite with acid formation. It produced an early acidity in milk with a subsequent alkalinity and agglutinated with the "Harris" serum in high dilutions.

The autopsies were obtained as soon as possible after death, the pieces of the organs placed in equal parts of 95 per cent. alcohol and 10 per cent. formalin. After from one to three days they were transferred to alcohol and mounted and cut in paraffin. The staining was done with hæmalaun and eosin, sections for bacteria were stained by the Gram-Weigert method and, for those negative to Gram, with borax-blue and differentiated with ½ per cent. acetic acid. The Weigert stain for fibrin was used to demonstrate fibrin.

The first seventeen cases were winter cases occurring between November 1st and April 15th, and the last fifteen summer cases, between May 1st and September 1st. There seems to be no difference in the histological findings, due to the time of year.

*This statement was true at the time it was written, but since then at least six cases of double infection in infants have been reported.

REPORT OF CASES.

Case I.—C. S., ten and one-half months old. Brought to the hospital and left without any history being obtained. Signs of broncho-pneumonia in both lungs. She did well with this and was apparently convalescent when, on the eighth day after admission, she began to vomit and have frequent mucous and bloody stools. These persisted till death, seven days later. Temperature at first, 100-101.5° F.; rose three days before death to 102-103° F., where it remained. The *B. dysenteriæ* was cultivated from the stools five days before death.

Autopsy.—There is a typical broncho-pneumonia in both lungs, degenerated kidneys, a large, soft hyperplastic spleen and a moderately fatty liver. Stomach normal as also small intestine, except for a slight follicular hyperplasia. The mucous membrane of the large intestine is congested throughout, and has lost its velvety appearance, but there is no thickening of the wall.

Microscopical.—There is a marked hyperplasia of the lymphoid follicles in the small intestine due chiefly to an increase in the lymphoid cells and less to an increase in the endothelioid cells. The hyperplasia extends into the surface mucosa, separating the crypts from each other, and densely infiltrating the stroma. Here there are occasional depressions in the mucosa extending into the enlarged follicles, at which points the mucous membrane is deficient. The submucosa is quite normal. A similar hypertrophy of the solitary follicles is found in the large intestine, with superficial epithelial defects but without reaction.

Bacteria.—There are few organisms in the sections, either positive or negative to Gram, and those seen are very near the surface.

Case II.—S. M., five months old. Taken sick on November 11th, and death occurred twenty-five days later. Stools were greenish with much mucus but no blood, occasionally watery, one to five a day. Temperature touched 100° F. only once, the rest of the time it was 99° F. or below.

The *B. dysenteriæ* (Shiga) was found two weeks before death at the first examination.

Autopsy.—Small intestine normal except for extreme lower end, where there is slight congestion. Large intestine—The mucosa is congested throughout, the lower part extremely so, where it is also thickened.

Microscopical.—Small intestine practically normal. Large intestine—The lesions, exclusive of edema and congestion of the mucous membrane, are insignificant. Slight lymphoid hypertrophy. Spleen—There is a moderate endothelial hyperplasia of the follicles.

Bacteria are found, chiefly bacilli negative to Gram, in the superficial part of the mucosa, in considerable quantity.

Case III.—N. D., ten months old. Admitted to hospital nine days before death, with diarrhea and with a temperature of 97° F. The stools were one to five a day, yellow and brown, with mucus and only once a little blood. He emaciated rapidly and was markedly so at death.

The *B. dysenteriæ* was cultivated from the mucous membrane of the colon at autopsy.

Autopsy.—Kidneys degenerated. Liver soft. The other organs are normal, except the colon, the mucous membrane of which is very much congested and the submucosa, on section, seems to be thickened. No apparent ulceration. The mesenteric glands are quite enlarged, but only slightly congested.

Microscopical.—Large intestine—The mucous membrane is much congested, though there are no hemorrhages. The lymphoid follicles are a little swollen. The submucosa is somewhat thickened from edema and superficial cellular infiltration, especially about the blood vessels. The muscular layer is normal.

Bacteria.—On the surface of the mucosa and between the epithelial cells a moderate number of organisms negative to Gram are seen, mostly bacilli of the size of colon bacilli, arranged in small clumps.

Case IV.—T. W., five months old. Was admitted to the hospital suffering from intestinal indigestion. During the first month he improved very much and gained some in weight, then developed a diarrhea and began to lose weight. A day or two afterward the first trace of blood appeared in the stools, only small in amount, but coincident with this a rise in temperature from 99° F. to 103° F., and this remained high, sometimes up to 104° F., till his death, eight days later. The stools toward the last showed no blood whatever, but were yellowish green, with much mucus, and there was also considerable abdominal rigidity and tympanites. The *B. dysenteriæ* was obtained by culture from scrapings of the intestinal mucosa.

Autopsy.—Liver—Great congestion, with fatty infiltration. Kidneys, congested and degenerated. Spleen congested. Lungs—Hypostatic pneumonia in both.

The peritoneal cavity contains cloudy serum. Between the loops of intestine there are some delicate bits of fibrin. There is no marked injection of the vessels and the peritoneum has lost only partially its normal shining appearance. Stomach normal. Small intestine appears normal except for slight swelling of Peyer's patches and the solitary follicles. Large intestine shows extensive changes, more marked at the lower end. The wall of the sigmoid and rectum is very much thickened. In the cecum the mucous membrane has lost is normal smooth appearance and is dotted over with granular areas and marked congestion. In the sigmoid and rectum the mucous membrane is covered with a grayish pseudo-membrane that strips off with difficulty, taking with it all structures down to the very much thickened submucosa. The mesenteric glands are moderately swollen and congested.

Microscopical.—Small intestine—The surface epithelium is partially denuded. The mucous membrane, excepting Peyer's patches, is apparently normal. Peyer's patches are moderately swollen, there being a hyperplasia of the lymphoid cells only. There is no necrosis of cells. The submucosa and muscularis are normal. Large intestine—Sections show a diffuse necrosis of the mucosa, varying in intensity; in some places only the superficial edge is necrotic, in others the necrosis extends through the entire depth and as far as the muscularis mucosæ. All the parts of the mucosa are affected, though the Lieberkühnian glands suffer especially. The blood vessels are either injected or closed by means of pink thrombi. These thrombi show little or no fibrin and appear to be made up of coalesced red blood corpuscles. The surface is not covered with a definite membrane, the necrotic tissue adheres to the subjacent living tissues in general, occasionally it is lifted up and gives the impression of being a pseudo-membrane. At the line of junction of the living and dead tissue there is an invasion of the latter by polymorphonuclear cells and a general increase of the cells in the mucosa. Nuclear fragmentation is not abundant. The solitary follicles exhibit a somewhat more marked hyperplasia than in the small intestine, the centers showing endo-

thelial proliferation. The mucosa over the follicles is deficient. The submucosa is edematous and contains a greatly increased number of mononuclear cells, with excentric nuclei, some of which are plasma cells. The muscular coat, except for the fibrous septa which show an increased number of mononuclear cells, is normal. There is a massive bacterial development in the necrotic mucosa and an extension of bacteria a certain distance into the adjacent living mucosa. The bacteria consist of forms staining with Gram and decolorizing by Gram; among these are cocci and innumerable bacilli. The invading organisms consist also of cocci and bacilli, among which are forms having the colon-typhoid morphology. Cultures from this case gave colon bacilli from the peritoneum and all the organs while, in addition, the *B. dysenteriæ* was obtained from the intestinal contents.

Case V.—G. C., four months old. Admitted to the hospital December 24th. Stools yellowish or greenish, two a day; no temperature till January 23d, then a trace of blood, with gradual rise of temperature to 102½° F. The stools, three to nine a day, contained mucus and blood. Death five days later. *B. dysenteriæ* obtained by culture from the scrapings of the mucosa of the colon.

Autopsy.—Organs practically normal, except the intestines. Small intestine—Follicles in the ileum prominent. Large intestine—In the cecum and ascending colon a number of solitary follicles are seen, slightly elevated above the mucous membrane. The mucous membrane is moderately congested in irregular areas, but otherwise appears quite normal. In the sigmoid and rectum the solitary follicles are distinctly ulcerated, showing pock-marked depressions, and the neighboring mucous membrane is congested. The mesenteric glands are moderately enlarged.

Microscopical.—Large intestine—The general mucous membrane is normal, except in the region of the solitary follicles, which are moderately enlarged and over which the mucosa is deficient. There is no marked cellular reaction, and the hyperlasia of the follicles is a lymphoid one. Other coats normal. Small intestine—There is a moderate hyperplasia of the follicles, which have enlarged endothelial centers. The submucosa and muscle are normal.

Bacteria.—Only a few bacilli negative to Gram are found on the surface and of those positive to Gram only an occasional one.

Case VI.—C. C., two years old. Had never been out of the institution. Three weeks before death he was discovered to be suffering from an acute nephritis; the urine contained 25 per cent. albumin, blood and casts. He was very edematous. It was impossible to find the cause, possibly a mild scarlatina that had been overlooked. The urinary condition did not change nor did the edema. He had green, loose, watery stools till six days before death, then he had mucous stools, but never any blood. The temperature at the end was between 100° F. and 104° F.

The *B. dysenteriæ* was isolated three days ante-mortem.

Autopsy.—The lungs are edematous, the liver fatty, the spleen congested. There is ascites and anasarca. The kidneys are enlarged, the capsules free, small hemorrhages are seen on the surface, the cortex is thickened and yellowish, the pyramids prominent, the consistency soft. Small intestine—The upper part is congested, the lower 150 centimeters are covered with a thick, almost continuous pseudo-membrane, most marked toward the valve; on stripping it off, all of the mucous membrane is removed with it. There are hemorrhages beneath

this membrane which ends exactly at the ileo-cecal valve. The whole wall of the intestine is very much thickened. The large intestine shows a few small patches of congestion and the follicles are enlarged. The mesenteric glands are enlarged and red.

Microscopical.—The kidneys show a marked degeneration of the epithelium; there are hemorrhages into the tubules which contain casts. Within the capsules of the glomeruli there is an exudation of albumin and there is beginning exudation into the kidney stroma. Ileum—The mucous membrane is almost completely necrotic; here and there are remains of imperfectly preserved crypts. The necrotic mucous membrane is demarcated from the submucosa by a layer of cellular fragments, by hemorrhages and by mononuclear and polymorphonuclear cells. At this level occasional small vessels are thrombosed. The submucosa itself is swollen, infiltrated with serum and fibrin, and shows here and there preserved and fragmented cells similar to those in the mucosa. The superficial muscular layer is infiltrated with small round cells. There is a massive development of bacteria in the necrotic tissue but there is no definite false membrane. In the colon there is congestion and hyperplasia of the follicles. There are scattered areas of very slight superficial necrosis, no ulceration, and between these areas the intestine is fairly normal.

Bacteria.—The surface and to a considerable extent the whole of the mucous membrane, but especially the remains of the glands, are closely packed with bacilli negative to Gram, which are scattered diffusely throughout and also collected in large masses.

Case VII.—J. M. The child was two years old and an imbecile. She was taken sick in the latter part of November with diarrhea. November 28th—No Shiga bacilli were found, but they were present on December 1st. She had diarrhea for one month and then recovered from this completely, but lost ground constantly and developed a very marked broncho-pneumonia, to which she succumbed on the 29th of January. For several weeks before her death her stools had been brown and normal, and examination failed to show the presence of any dysentery organisms.

Autopsy.—There is a very marked broncho-pneumonia, with beginning abscess formation. The stomach and small and large intestines appear normal but for congestion. No hemorrhages, no ulceration, no follicular swelling, and the mucous membrane is smooth and glistening.

Microscopical.—Ileum—Slight congestion. No ulceration, no necrosis, moderate infiltration of the interglandular stroma, with mononuclear cells, practically no polynuclear. This infiltration extends down to the submucosa, which is unaffected. Colon—The changes are the same as in the ileum. The cellular infiltration is a little more marked. Almost all the cells lining the crypts have been transformed into "goblet" cells. The solitary follicles are unaffected.

Bacteria.—Very few of any kind are found, and those are superficial in the extreme.

Case VIII.—G. F., one year old. Was admitted to the hospital suffering from diarrhea, which he had had for some days. Death nineteen days later. Temperature the first few days 100-101° F., rising again just before death. Stools, two to five a day, green or brown and watery, with flakes of mucus, never any blood.

The *B. dysenteriæ* found two weeks before death and again at autopsy.

Autopsy.—Lungs, hypostatic pneumonia. Liver, very fatty. The follicles of the spleen are prominent. Pancreas and kidneys negative. Small intestine—Minute superficial erosions of the solitary follicles and Peyer's patches are seen. There is the same condition of the follicles in the colon. No ulceration.

Microscopical.—Ileum—The follicles are hyperplastic and there is very superficial ulceration over them, with consequent depressions. Large intestine—The general mucosa, except in the neighborhood of the follicles, appears normal. The follicles themselves are considerably enlarged, the enlargement being due chiefly to an increase in the endothelial elements occurring both in the center of the follicles and in the periphery. The neighboring mucosa is infiltrated with endothelial cells and there is a central depression which extends into the follicle, at which point the epithelium is deficient. The submucosa and occasionally just beneath this the muscularis show a distinct cellular infiltration, the cells being of the mononuclear variety. The muscle is normal.

Bacteria.—Bacilli negative to Gram are found in considerable number, extending quite deeply in apparently healthy tissue toward the submucosa.

Case IX.—S. T., one year old. In January she had bronchitis. Began on February 7th with broncho-pneumonia. Five days later, up to this time having been constipated, she developed diarrhea, with blood and mucus in the stools, which were four to five a day. The temperature was falling till the intestinal symptoms developed, then it rose and remained continuously high, 101° F. to 103° F. till death, six days later. Two days after admission the stools were examined and were negative. Five days before death, that is one day after the diarrhea developed, the examination was positive for Shiga bacilli.

Autopsy.—Lungs—Broncho-pneumonia. All other organs negative but the colon; the mucous membrane of the lower two-thirds of this is much thickened, appearing edematous and congested.

Microscopical.—The mucous membrane of the colon is, in general, well preserved. There is a transformation of many of the cells in the crypts into "goblet" cells and some of these crypts are dilated, so as to be three or four times as large in diameter as the normal ones. There is a slight general congestion. The follicles are moderately enlarged, due to a proliferation of endothelial cells. No ulceration and no infiltration of the coats with cells. The submucosa and the muscularis are normal.

Bacteria.—Organisms positive and negative to Gram infiltrate the mucous membrane to no very great depth and in small numbers.

Case X.—R. W., age three years. Admitted December 31st. Death February 1st. Diarrhea constant, stools watery and foul until three weeks before death, then blood and mucus were noticed. Temperature occasionally 101° F. to 103° F., falling shortly to normal.

The *B. dysenteriæ* was isolated three weeks and again two weeks before death.

Autopsy.—Lungs—Marked broncho-pneumonia. Liver—Large and fatty. Stomach—Congested throughout. Small intestine—Congested and follicles prominent throughout. Large intestine—Markedly congested, with rough, granular appearance and superficial ulcerations.

Microscopical.—Ileum—The mucous membrane is congested and the lymphoid tissue hyperplastic. Large intestine—The mucous membrane is in places greatly modified. In these parts the granular structures are invisible. The mucous mem-

brane consists of small cells and remains of crypts which are much compressed. On the surface there is a necrotic pseudo-membrane consisting of filaments of fibrin and desquamating necrotic cells. The submucosa and muscularis appear quite normal. An additional section of this part shows in addition to this pseudo-membrane a fair number of polymorphonuclear cells and cellular fragments.

Bacteria.—In the pseudo-membrane there are many organisms, chiefly cocci positive and bacilli negative to Gram's stain, the latter predominating, but they do not invade the tissues to any great depth.

Case XI.—H. S., one year old. Admitted to the hospital March 1st. He had been in the hospital a month before suffering from diarrhea and anemia, but had been discharged in good condition. His temperature on admission was 102° F., and this dropped to normal for one day, but rose again irregularly to 104° F. and remained there until his death, six days later. His stools were three to four a day, green, with mucus and occasionally blood. There were marked meningeal symptoms.

The *B. dysenteriæ* was cultivated from the stool five days before death.

Autopsy.—Lungs and spleen congested. Liver extremely fatty. Stomach normal. Small intestine—Peyer's patches and the solitary follicles are a little enlarged and present a "shaven beard" appearance. Large intestine—Congested, especially at the lower end, and the follicles are prominent.

Microscopical.—Small intestine—The ileum is in an excellent state of preservation. Large intestine—There is congestion of the mucosa. Almost all the epithelial cells of the crypts are "goblet" cells. The lymphoid tissue of the solitary follicles is hyperplastic. The submucosa and muscularis are normal. The mesenteric glands are congested.

Bacteria.—Sections stained for organisms show practically none positive to Gram; negative to Gram there are a moderate number, superficially situated, and of these a few are of the colon size and form.

Case XII.—M. M., ten and one-half months. Had been very ill for one month with nasal diphtheria, double otitis and cervical adenitis. Eight days before death he had a chill and a rise of temperature, followed by pulmonary signs. The temperature went up to 104° F. and remained high till just before death, when it dropped rapidly. Seven days before death mucus appeared in the stools, but there never was any blood. A culture from scrapings of the mucosa of the colon gave a growth of the *B. dysenteriæ* (Shiga).

Autopsy.—Lungs—Marked pneumonia of the right lung, with empyema. Liver, fatty. Spleen, large and soft. Stomach, post-mortem digestion. Small intestine, negative. Large intestine, no ulceration, no congestion. Mesenteric glands enlarged.

Microscopical.—Ileum normal. Colon—The mucous membrane throughout is practically normal. There is no congestion and no infiltration. The submucosa and muscular layers are normal. The follicles are intact and not hyperplastic. Spleen—Very marked proliferation of the endothelial centers of the Malpighian corpuscles.

Bacteria.—Very superficial and few in number.

Case XIII.—J. W., two months old. Was admitted to the hospital March 25th with pneumonia. Died April 3d. He had one to three yellow and green stools a day, no mucus and no blood. The temperature was normal throughout.

Five days before death no Shiga bacilli; two days before death the bacilli were isolated.

Autopsy.—Lungs typical and very marked broncho-pneumonia. Spleen large, dark red and soft. Liver and kidneys degenerated. Stomach normal. Small intestine—There are congested Peyer's patches and the solitary follicles are pigmented and present a typical "shaven beard" appearance, most marked low down. Large intestine is slightly congested and the follicles prominent.

Microscopical.—Ileum—The solitary follicles and Peyer's patches are a little enlarged from an increase of the lymphoid cells; except for this the appearance is normal. Large intestine—The mucous membrane is in an excellent condition of preservation. The follicles are slightly swollen; no other changes.

Bacteria.—These are very few and very superficial.

Case XIV.—M. T., eighteen months old. An enormously rachitic child, with bronchitis and beginning pneumonia. Was admitted March 11th and died March 17th. Constipated most of the time till two days before death, when the stools became merely mucus, with blood, and *B. dysenteriæ* was found.

Autopsy.—Lungs—Beginning broncho-pneumonia. Small intestine—Congestion in the lower half of the ileum, with the solitary follicles and Peyer's patches slightly enlarged. Large intestine—Intense congestion of the mucous membrane of the entire colon. No ulcers.

Microscopical.—Small intestine—The agminated follicles are much swollen, the centers converted into large germinal centers with an endothelioid center and in the periphery the endothelial cells are also increased. The mucosa is complete over these swollen follicles. The submucosa and muscle appear normal. Large intestine—In all of the crypts are numerous "goblet" cells. Distinct hemorrhages have taken place into the mucosa. In the neighborhood of one of these hemorrhages there is an area of necrosis that extends to the submucosa. Where this occurs the staining of the cells is absent and the tissues are disintegrated. A large number of bacteria are in this area, but no reaction is present. The submucosa is intact.

Bacteria, both positive and negative to Gram's stain, are present on the surface, but in the necrotic areas they are found in countless numbers.

Case XV.—A. C. Admitted to the hospital at the end of a pneumonia, with râles the only signs in the chest. She had diarrhea, stools two to four a day, green with mucus. Never any blood. The temperature never went above 100° F. Two days before death *B. dysenteriæ* (Shiga) was obtained from the stools.

Autopsy.—Liver and kidneys degenerated. Spleen congested. The other organs, including the stomach, are normal. Small intestine—The solitary follicles and Peyer's patches are a little swollen and appear slightly ulcerated; the lower two inches of the ileum are congested and changes there are more marked. Large intestine—All the follicles are prominent and many, especially in the lower portion, are dimpled. The whole wall in the lower six inches is much thickened and the mucous membrane is pale, rough and granular and looks necrotic. The mesenteric glands are enlarged.

Microscopical.—Small intestine—There is denudation of the surface epithelium and much breaking up of the mucous layer. The agminated nodules are swollen; the swelling consists in a moderate lymphoid hyperplasia without necrosis. The general mucous membrane is normal in appearance. The submucosa is moderately infiltrated with mononuclear cells, of which some show

excentric nuclei. Large intestine—The mucous membrane is thin, with a great deficiency in the crypts of Lieberkühn. The solitary nodules are prominent but not markedly enlarged. The superficial mucosa in many places refuses to stain and in others the staining is absent or poor below the muscularis. Fragments of nuclei are occasionally seen in the non-staining portion, but there is a striking absence of leucocytic reaction in the adjacent living tissue. The mucosa shows a cellular infiltration similar to, but more intense than, that in the small intestine. The spleen is congested and the germinal centers of the Malpighian bodies show endothelial hyperplasia.

Bacteria.—When stained for micro-organisms a moderate number of Gram positive bacteria are found. The Gram negative bacilli of colon morphology extend deeply into the tissues. The necrotic areas are closely packed with them and even the submucosa contains a decided number in its more superficial part, especially around the blood vessels.

Case XVI.—R. G., thirteen weeks old. Admitted at five weeks old for malnutrition. Had gonorrheal ophthalmia and gonorrheal joints. Never any mucus or blood in the stools and always a subnormal temperature. Stools, two to six a day, thin, yellow or green. *B. dysenteriæ* was found two weeks before death.

Autopsy.—Lungs—Beginning broncho-pneumonia. Stomach, duodenum and jejunum, normal. Ileum—Peyer's patches pigmented, otherwise not affected. Large intestine—The upper half congested, the remainder normal. The mesenteric glands not enlarged. Liver congested. Spleen firm and hard.

Microscopical.—Small intestine—No changes. Large intestine—There is slight congestion, otherwise all the coats are normal.

Bacteria.—Very few of any kind and those superficially situated.

Case XVII.—J. K., three and one-half months old. Was admitted to the hospital suffering from malnutrition and indigestion. Did fairly and gained a little for a time. Then began to have frequent stools, about five a day, that, eight days before death, contained mucus, never any blood. The temperature for eight days of the disease was from 101° F. to 103° F.

The *B. dysenteriæ* (Shiga) was found eight days before death.

Autopsy.—Spleen—Congested and enlarged. Lungs—Hypostatic pneumonia. Stomach, normal. Small intestine, congested, with swelling of Peyer's patches. Large intestine, intense congestion throughout; no ulcerations made out; follicles swollen.

Microscopical.—Ileum—Surface columnar epithelium mostly denuded. The mucosa, excepting lymphoid structures, appears normal. The agminated nodules are swollen and there is a general hyperplasia of the lymphoid cells and a marked proliferation of the endothelial cells of the germinated centers. All other structures are normal. Large intestine—The changes are similar to those in the small intestine; no ulceration.

Bacteria.—Very few of any kind are found.

Case XVIII.—A. H., aged seven months. Was brought to the hospital with a history of three days' diarrhea. The child was very fat but very rachitic. She died on the twelfth day of the disease. The stools were three to seven a day, green, with much mucus, never any blood. The temperature was irregular, 99° to 102° F., rising just before death. Was given 10 c.c. of "Harris" serum,

with temporary improvement but no lasting benefit. The *B. dysenteriæ* was isolated from the stools ante-mortem.

Autopsy.—Lungs—Lower lobes congested. Liver large and fatty. Stomach, duodenum and jejunum normal. Ileum congested irregularly in the lower eighteen inches. Large intestine—Congested in patches throughout its whole extent and has partly lost its smooth appearance. The mesenteric glands are not enlarged.

Microscopical.—The lymphoid tissue of the lower ileum and colon is slightly hyperplastic. Except for this there are no marked histological changes.

Bacteria.—A few cocci and bacilli are found in the superficial mucosa.

Case XIX.—B. F., aged nine months twenty-seven days. Was brought to the hospital in bad condition, with diarrhea and without any accurate previous history. Was very emaciated, had meningeal symptoms, stiff neck, irregular pupils and internal strabismus. The stools most of the time were yellow, occasionally green, with a trace of blood, two to five a day. The temperature at first was below 100° F., rising irregularly to 104° F. just before death. The duration of illness in the hospital was fourteen days. *B. dysenteriæ* was isolated three days before death.

Autopsy.—Lungs edematous. Liver very fatty. Stomach normal. Small intestine—Upper part normal. In the lower two feet Peyer's patches are enlarged, with small superficial ulcerations over them. Large intestine—There is congestion most marked in the neighborhood of the ileo-cecal valve. The solitary follicles are dimpled. The changes are slight in the descending colon and sigmoid. The mesenteric glands are slightly enlarged.

Microscopical.—Small intestine—The general mucosa shows little alteration. As the confines of the swollen lymphoid nodules are approached the villi are swollen and rendered more obtuse by an increase of the lymphoid cells. The lymphoid masses are markedly enlarged, the new cells being of the lymphoid habitus. From the center of the mass there is a funnel shaped depression in which the lymphoid cells often stain poorly and over which the mucosa is imperfect. The submucosa and muscle show no striking alteration. There is no striking change in the mucous membrane of the large intestine, but the solitary nodules are enlarged in a manner similar to that described in the small intestine and over them the epithelial layer is deficient.

Bacteria of any form or staining properties are few in number.

Case XX.—R. A., nine months twenty-six days. Was brought to the hospital in poor condition with Bednar's aphthæ. He had stools, three to six a day, very foul, green, with mucus, occasionally a little blood. There was a moderate temperature. He emaciated gradually and died marantic after two and a half weeks in the hospital.

The *B. dysenteriæ* was obtained by scraping the mucous membrane at autopsy.

Autopsy.—Lungs—Tubercles scattered throughout both. Bronchial glands cheesy. Liver fatty. Spleen small and soft, with tubercles on surface and on section. Stomach, duodenum and jejunum negative. Ileum—Lower foot congested. In the lower two inches the Peyer's patches are reddened and swollen. Large intestine—Upper one-eighth of colon irregularly congested. Lower seven-eighths, much congested and a yellow stringy material is irregularly distributed

over and adherent to it. Follicles apparently not affected. Mesenteric glands slightly swollen and reddened.

Microscopical.—Large intestine—The mucosa is thickened, the thickening being due to cellular products on the surface of the mucosa. These cells are desquamated epithelium and other surface cellular elements which cover the crypts to a considerable depth. The crypts themselves are of quite normal appearance. The submucosa and muscle are normal. The solitary follicles are swollen, but not markedly so. In the small intestine there is a similar desquamative condition of the surface cells and in addition a moderate enlargement of the agminated follicles due to an increase of lymphoid cells. No changes in the submucosa.

Bacteria.—Bacilli negative to Gram are found in the superficial portion of the mucosa in small numbers and in rather greater numbers among the desquamated epithelial cells.

Case XXI.—J. S., seven months twenty-four days old. A well nourished child; began to be ill acutely, with temperature 103° F., rising in twenty-four hours to 104.5° F. The stools at first were brown and loose, two to four a day. The temperature then dropped to normal and after three days the stools were normal for twenty-four hours. Following this a rise of temperature to 103° F. and the stools became frequent and green, with mucus and blood. Death five days later despite the injection of 10 c.c. of "Harris" and 10 c.c. of "Seward" serum. Temperature for the last three days 100-102° F. *Bacillus dysenteriæ* was isolated from the stools five days before death and was also found post-mortem from the scrapings of the mucous membrane of the colon.

Autopsy.—Lungs—Slight congestion in the lower lobes. Liver fatty. Spleen small and firm. Stomach normal. Small intestine—Lower six inches slightly congested. Large intestine—Congested and in places there are small hemorrhages into the mucosa. The mucous membrane, especially near the ileo-cecal valve, presents very small superficial yellowish areas of apparent necrosis.

Microscopical.—Small intestine practically normal. Large intestine—Throughout its whole extent there is congestion. In the sections from the neighborhood of the ileo-cecal valve the blood vessels of the mucosa and submucosa are enormously dilated; in the former situation there are actual hemorrhages. There are small areas near the hemorrhages whose cells stain poorly and there is actual, although superficial, loss of substance. There is considerable inflammatory reaction around these areas. The submucosa is much infiltrated with mononuclear cells, especially in the superficial portion. The muscularis is normal. In other parts of the colon the changes are less marked.

Bacteria.—Cocci and bacilli, positive and negative to Gram, are found in great numbers in the neighborhood of the necrotic portions. No especial type seems to predominate.

Case XXII.—M. B., eleven months twenty-six days old. While in the institution suffering from measles she had had a diarrhea, with numerous green mucous stools, no blood. The *B. dysenteriæ* (Shiga) was then isolated from the stools. Two weeks later she developed diphtheria of the pharynx and larynx, with consecutive broncho-pneumonia. Death one week after the first signs of diphtheria.

Autopsy.—Tonsils, pharynx, epiglottis, larynx and vocal cords covered by a greenish-brown false membrane. Lungs—Left lower lobe is consolidated with

hemorrhages into the pleura. Liver very fatty. Spleen large and soft. Stomach, duodenum and jejunum normal. Ileum—Peyer's patches in the lower portion are reddened and covered with a small amount of adherent yellowish material. Remainder normal. Large intestine—The congested mucous membrane is thickened in spots, with small ulcerations. The follicles show superficial erosions, especially in the sigmoid.

Microscopical.—Large intestine—The general mucosa appears normal. The follicles are enlarged, the hypertrophy being due chiefly to lymphoid cell increase and the adjacent submucosa is infiltrated with small cells. In the neighborhood of the follicles, but more or less independent of them, are ulcers of small diameter that extend often to the submucous coat. Covering these ulcers and the adjacent surface of the mucosa is a fibrinous cellular exudate which is closely adherent. The submucosa in the neighborhood of the ulcers and even at a distance shows a strong mononuclear infiltration. The other coats are normal. Small intestine—There is a marked hypertrophy of the follicles, with a similar fibrino-cellular covering upon the adjacent mucous membrane. The general submucosa is less invaded than in the large intestine.

Bacteria very few of any kind.

Case XXIII.—M. K., five months twenty-two days old. She entered the hospital with a history of diarrhea and general malnutrition. She was in the the hospital twelve days. Temperature, 99-100° F. Stools four to five a day, green, with mucus. Blood first appeared one week before death and on the last day was very abundant. The *B. dysenteriæ* was isolated ten days before death.

Autopsy.—Lungs, beginning broncho-pneumonia. Liver fatty. Spleen small and firm. Stomach normal. Duodenum and jejunum normal. Ileum—Small areas of congestion, no ulceration or involvement of the lymphoid tissue. Large intestine—Slight irregular congestion. Few prominent follicles.

Microscopical.—Except for a moderate congestion there are no histological changes in the small or large intestine.

Bacteria of any description are very scanty.

Case XXIV.—H. L., aged one year four months. Brought to the hospital with signs of pneumonia over the left lower lobe, which constantly extended, and a temperature of 104° F. Very ill from the start and had five to eight stools a day, green, with mucus, but no blood. Temperature dropped after six days to 99° F., but rose again to 102° F. to 103° F., and remained there till death, twenty-one days later. *B. dysenteriæ* was obtained by scraping the mucosa post-mortem.

Autopsy.—Lungs—Broncho-pneumonia scattered in both lungs. Bronchial glands a little enlarged; no signs of tubercle. Liver large, soft and pale. Spleen large and soft. Kidneys soft and pale. Stomach, duodenum and jejunum normal. Ileum—Peyer's patches swollen and congested. Large intestine congested throughout, with some loss of luster, which is most marked low down and in the region of the ileocecal valve. Follicles not prominent. Mesenteric glands much enlarged and caseous, tubercle bacilli demonstrated by staining. No other tuberculous lesions found.

Microscopical.—Small intestine—Congestion and moderate hyperplasia of the agminated follicles. Large intestine—The mucous membrane in general is normal. There is a transformation of many of the cells in the crypts into "goblet"

cells, with subsequent dilatation of the crypts to four or five times their normal diameter. The other coats are normal.

Bacteria.—Very few of any kind seen, and these are very superficial.

Case XXV.—C. B., eight months twenty-two days old. A poorly nourished child, with indefinite signs in his chest, was admitted to the hospital with diarrhea, which persisted till death, twenty-eight days later. The stools, four or five a day, were green and yellow, with mucus, occasionally a trace of blood. Temperature, 98°-100° F. Emaciated rapidly. *B. dysenteriæ* was isolated seven days before death.

Autopsy.—Lungs—There are fresh tubercles on the visceral pleura, but the parietal pleura is normal. The left apex contains numerous caseous tuberculous masses, together with small fresh tubercles. The bronchial glands are enlarged and cheesy. Liver fatty. In the spleen are small fresh tubercles. Stomach normal. Duodenum and jejunum normal. Ileum—The Peyer's patches are enlarged and ulcerated, the edges of the ulcers thickened and they extend deeply into the muscular coat. They are round, not longitudinal or perpendicular to the long axis of the gut. While their general appearance is tuberculous no tubercles are seen on the peritoneal coat. Large intestine—All the solitary follicles appear enlarged and the edges of many are congested. The majority are slightly pitted. The mesenteric glands are enlarged and caseous.

Microscopical.—There are tuberculous processes in both the small and large intestine, which so obscure the other lesions that it is not considered advisable to draw any conclusions from this case.

Case XXVI.—V. M., six months nineteen days old. A poorly nourished child; was admitted to the hospital with a history of several days' diarrhea. He was under observation five weeks, with practically a normal temperature, rising occasionally to 102° F. The stools were fluid and green, two to five a day, no blood, but slight amount of mucus. *B. dysenteriæ* was isolated from the stools on the day of admission.

Autopsy.—Liver large and soft. Spleen hard and small. Small intestine—Peyer's patches congested; no ulceration. Large intestine—The mucous membrane near the ileo-cecal valve is congested; throughout the rest of the colon the follicles are pigmented and slightly depressed.

Microscopical.—Owing to the length of time of the autopsy after death, post-mortem changes had taken place in the intestines that made them unsuitable for microscopical examination.

Case XXVII.—C. C., seven months. There was a history of two days' diarrhea before admission to the hospital. The stools were green with mucus, two to six a day. No blood till two days before death, after an illness of thirty-four days. Temperature 98° F. to 101° F., until just before death, then a rapid rise to 104° F., followed by a fall. The Shiga bacillus was not found twenty-eight days before death; an examination for it was positive eighteen days before death.

Autopsy.—Liver fatty. Spleen firm and dark. Stomach normal. The small intestine appears normal except the last two inches of the ileum, which are greatly congested. One small spot the size of a pea is thickened, exfoliating and covered with a necrotic mass. The large intestine is very much thickened throughout its whole extent, apparently due to a swelling of the submucosa. There is congestion throughout In places extending for two to three inches there are

hemorrhages into the mucosa. In no place does the mucous membrane appear smooth. No ulceration is made out, no follicular enlargement. The mesenteric glands are a little enlarged.

Microscopical.—The lower ileum at one point is greatly modified. The structure of the mucosa is almost obliterated on account of great swelling of the villi and the greatly diminished staining power of the cells. In places, however, the crypts are fairly preserved. There is much congestion and definite hemorrhage into the tissues. Overlying the mucosa and attached to it in a definite locality is a necrotic pseudo-membranous mass containing fibrin and desquamated and emigrated cells. The muscularis mucosæ is preserved practically intact but the submucosa is swollen, infiltrated with serum and mononuclear cells, the blood vessels being injected. The muscular coat appears normal as does the peritoneum. Colon—The mucosa is fairly normal, although there are hemorrhages into it, at which points the staining of the cells is very imperfect. The hemorrhages extend into the submucosa, which is swollen, containing an excess of mononuclear cells, though it is much less affected than the submucosa of the small intestine described.

Bacteria.—There is a massive bacterial growth in the pseudo-membranous mass as well as in the mucosa of the lower ileum and colon. Organisms, cocci and bacilli are found in great numbers, but the bacilli of the colon habitus and staining qualities predominate, especially in the mucous membrane, where they extend as far as the muscularis mucosæ but no deeper.

Case XXVIII.—M. H., eight months old. Ill ten days with diarrhea. Stools one to seven a day, green and fluid, with mucus; no blood. Temperature, 98°-102° F., only reaching this latter figure once. She lost flesh rapidly and died marantic. *B. dysenteriæ* (Shiga) was isolated from the stools three days before death.

Autopsy.—Liver fatty. Spleen, small, soft, atrophic. Stomach negative. Small intestine negative except for "shaven beard" appearance. Large intestine—Follicles a little prominent and pigmented. No ulceration. Mesenteric glands not enlarged.

Microscopical.—Ileum and colon present no marked histological changes.

Bacteria practically absent.

Case XXIX.—L. U., eight months eight days old. A very poorly nourished child, was admitted to the hospital in a moribund condition, with a normal temperature, but with frequent green fluid stools, containing mucus and blood. Death two days later. Temperature 104° F. at death. The *B. dysenteriæ* was isolated the day before death.

Autopsy.—Liver very fatty. Spleen atrophic. Stomach, duodenum and jejunum normal. Ileum—The Peyer's patches are pigmented; otherwise normal. Large intestine—The mucous membrane appears normal. A few follicles near the ileocecal valve are prominent.

Microscopical.—The mucous membrane of the ileum and colon, as, in fact, all the coats, are quite normal. In the colon there is slight hyperplasia of the lymphatic tissue.

Bacteria.—There are very few organisms of any kind discernible and these are most superficial.

Case XXX.—M. W., four months six days old. A fairly nourished child, with a history of four days' diarrhea; was admitted to the hospital in a condition of

extreme prostration. The stools were frequent and green, with a slight amount of mucus and, just ante-mortem, a trace of blood. She had a very slight temperature, varying from 98°-100° F. She took nourishment poorly and vomited what she did take. Death three days later. The *B. dysenteriæ* (Shiga) was obtained by scraping the intestinal mucosa post-mortem.

Autopsy.—Liver soft and fatty. Spleen normal. Stomach, duodenum, jejunum and ileum normal. Large intestine—Congestion throughout, but more intense in the cecum and sigmoid. No ulcerations. Follicles are not affected.

Microscopical.—Ileum normal. Large intestine—The mucosa is congested, the blood vessels widely dilated with blood, but there are no hemorrhages, and except for this, quite a normal histological appearance.

Case XXXI.—J. R., fifteen months old. Had suffered for months previous from malnutrition and vomiting. Admitted at the age of ten months. Weight seven pounds and fifteen ounces. Improved slowly and one month later was taking food well and gaining in weight. Then vomiting occurred and he lost weight though the stools were normal. Three months after admission the stools became loose, four to six a day, no blood, but later a little mucus and undigested food. This condition persisted for a long time, and twenty-nine days after the beginning of the diarrhea the *B. dysenteriæ* (Shiga) was obtained from the stools. Two days later the bacillus was not found and at the autopsy three weeks later it could not be recovered by scraping the mucous membrane of the colon. The child emaciated constantly and died in a condition of extreme marasmus, weighing but six pounds four ounces.

Autopsy.—Lungs congested. Liver small and dark. Spleen dark red, follicles prominent. Stomach and duodenum normal. Jejunum contained two small ulcers. Ileum—Peyer's patches are slightly swollen and a few small ulcers are present in them. Colon—Here are many ulcers extending through the mucosa and even down to the muscular coat, but the peritoneal surface is everywhere quite smooth. The ulcers are irregularly oval or round, with raised edges, and are not limited to the solitary follicles, which are not enlarged.

Microscopical.—Small intestine—The ulcers are relatively superficial and involve the layer of the crypts, but do not extend through the mucosa. The base consists of granulation tissue diffusely spread out, extending beyond the limits of the ulcer and invading the adjacent mucous membrane, the crypts of which are widely separated, and also invading at a distance the submucosa. The muscular coat escapes. Large intestine—The chief lesion is an ulcerative one, affecting the mucous membrane and to a marked extent the submucosa. The ulcer is clear, the base of it consisting of granulation tissue in a state of advanced formation. The superficial edge of the ulcers presents a reticulated appearance due to a superficial necrosis of the granulation tissue in which are fibrin and degenerated mononuclear cells. Where the glands are retained many have become dilated so as to form small cysts. The spleen is interesting in showing a marked endothelial transformation of the germinal centers of the Malpighian bodies.

Bacteria.—A very few cocci and bacilli are found on the surface of the ulcers as well as in the mucous membrane.

Case XXXII.—R. M., five months old. Was nursed for one month and after that fed on diluted cow's milk. For eight days she suffered from vomiting and diarrhea. There was a slight irregular temperature. In the hospital six days

with constant diarrhea, stools green or yellowish and watery, occasionally mucus, no blood. Died very poorly nourished. The *B. dysenteriæ* was isolated from the stools five days before death and again at autopsy, from scrapings from the colon.

Autopsy.—Liver moderately fatty. Spleen small, dark and firm. Stomach normal. Small intestine—Many small ulcers extending through the mucosa only and not limited to the solitary follicles. These are present in the duodenum, jejunum and ileum. Almost all the Peyer's patches are swollen and contain several small ulcers. No deep ones. Large intestine—The solitary follicles are a little enlarged, no ulceration. Mesenteric glands, slightly swollen and gray.

Microscopical—The small intestine shows a general hyperplasia of Peyer's patches, the enlargement being due partly to an increase of lymphoid cells and partly to endothelial transformation of the germinal centers. The mucosa in the neighborhood of these large follicles shows an increase in lymphoid cells. The ulcer examined microscopically within a Peyer's patch extends about half way through the mucous membrane though the cells of the patch are degenerated throughout. The surface of the ulcer is covered by a fibrinous and cellular exudate and the vessels within that portion of the mucosa are thrombosed. The submucosa shows an infiltration of the lymphoid cell type. Large intestine.—There is a "goblet" cell transformation of the epithelium. The spleen presents an endothelioid transformation of the germinal centers.

Bacteria.—Only a few and those superficially situated.

From a study of these tabulated cases it seems that they fall with considerable accuracy into several different groups according to the histological findings. Group A, comprising cases 4, 6, 10, 22 and 27, represents the most severe changes met with, which are more like those found by Flexner and Strong in the adult dysenteries of Manila than any I have to report. In these cases the change is a pseudo-membranous one, though the membrane is by no means continuous, but of irregular distribution in cases 10, 22 and 27; in cases 4 and 6, however, it is very extensive—in 4 in the colon and in 6 in the ileum. This pseudo-membrane is composed chiefly of necrotic tissue, desquamated cells and countless bacteria. Fibrin plays a very small part in it —two of the cases, and those the most intense, 4 and 6, showing none at all. There is necrosis of the mucosa in all these cases, and it is this chiefly which gives the appearance of a false membrane, but the necrosis does not extend beyond this coat. In this necrotic tissue and at its border there are hemorrhages and thromboses, and it is divided from the healthy tissue by a zone of mono- and polynuclear cell infiltration.

The submucosa in four of the cases of this group is much affected, it is swollen both from edema and from cellular infiltration. This

infiltration is composed of mononuclear cells, many with the excentric nuclei, characteristic of plasma cells, and is found most marked about the blood vessels. The submucosa in the fifth case is unaffected. The muscular coat is spared except for a slight mononuclear infiltration along the fibrous septa in one case and the peritoneal coat is normal save in the case of peritonitis.

It is interesting to note in this connection that though such cases in adults run, as a rule, very acute courses one of these children lived eighteen and two, twenty-one days after the bacillus was isolated from the stools, while the other children survived only six and eight days after the stools contained mucus or blood.

Two cases, 6 and 22, were so-called "terminal infections," occurring in nephritis and measles, respectively, the latter being also complicated by diphtheria.

In Group B, comprising cases 1, 5, 8 and 19, we find a different picture. Here the mucous membrane in both small and large intestines is, in general, in a good state of preservation; it is the lymphoid elements that suffer. In three cases both small and large intestines were involved in the process, in the fourth only the colon. The change consists in a hyperplasia of the lymph follicles, both agminated and solitary, and this hyperplasia is lymphoid in three of the cases and endothelioid in the fourth. The elements of these follicles show a tendency to invade the surrounding tissue. Over these follicles there is a deficiency of the epithelium and more or less excavation of the follicles themselves, causing the well-known "pitting."

The submucosa was in all cases approximately normal nor did the muscular or peritoneal coats show any change.

The case of Park and Carey,[10] the only autopsy in an infant suffering from undoubted Shiga infection that I have been able to find reported up to this time, evidently belongs to this group, the lesions being chiefly in the solitary follicles.

Of this group three of the infants were known to have been ill for fourteen days or over, and the fourth had diarrhea for only five days, but before this his stools were green and rather numerous and had not been examined, so that it is possible that the bacillus was present for a longer time. These changes are what one would expect in subacute cases with a more delayed termination, and, as mentioned above, this is true of three of the cases at least and possibly of the fourth. Case 1 was a terminal infection secondary to a broncho-pneumonia; the other three were primary cases.

Group C includes those cases characterized by superficial necrosis

and ulceration in the mucous membrane, not limited to the follicles, as in Group B, and not accompanied by the formation of a pseudo-membrane as in Group A. Of this group there are five examples, viz., 14, 15, 20, 21, 32.

The changes here consist in congestion and hemorrhage into the mucosa, with necrosis of isolated portions of the mucous membrane, which necrotic portion may be exfoliated so as to form ulcerations on the surface. The necrotic area and ulcerations are usually surrounded by a zone of inflammatory reaction. The lymphatic tissue shows more or less participation in the process. The submucosa escapes, with the exception of the one case where there is a cellular infiltration. The other coats are unaffected.

Two of these cases were very acute, lasting but two and eight days, respectively, while each of the others ran a course of about two weeks.

Cases 14 and 15 were terminal infections secondary to pneumonia.

The Group D, embracing those cases that show microscopically but few discoverable lesions, is a large one, including cases 2, 3, 9, 11, 12, 13, 16, 17, 18, 23, 24, 28, 29 and 30. Several facts may contribute to account for this. I have not considered the loss of the superficial epithelium as a pathological lesion and have regarded only loss of substance as true and not an artifact when it has been surrounded by a definite reactionary zone. The autopsies in most of the cases, unfortunately, could not be obtained immediately after death, as they should be, to draw any definite conclusions from the condition of the superficial epithelium. Loss of substance occurs so easily that in order to avoid false conclusions the above outlined plan was adopted. It is possible that autopsies obtained a few minutes after death will allow of some positive deductions in regard to the epithelial coating. Then too, the microscope fails to help us very much in the vascular changes in the mucosa on account of the various processes to which the tissue has to be subjected in the course of hardening, and for this reason the macroscopic examination probably gives us a truer conception of the amount of congestion. And, lastly, five cases of this group were terminal infections occurring in children suffering from serious and even fatal diseases, and others were in badly nourished institutional infants, to whose marasmus the infection with the Shiga bacillus was terminal. The infection was of a comparatively short duration and their reaction undoubtedly poor. Beyond congestion, moderate hyperplasia of the lymphoid tissue and in one case a little cellular infiltration of the superficial portion of the submucosa, there was very slight histological change.

Case 31 presents lesions quite distinct from any of the others. The ulcerations were very deep and were in the process of repair, death being due to marasmus after all intestinal symptoms had ceased and the Shiga bacillus had disappeared from the stools, nor could it be found post-mortem by scraping the mucosa.

Cases 25 and 26 could not be included in any of the groups owing to their unsatisfactory microscopical examinations, while case 7 is worthy of special mention, though presenting practically no abnormal change, on account of the fact that the child had recovered completely from the original infection only to fall a victim later to pneumonia.

From the foregoing it will be noticed that the severe cases are decidedly in the minority. The lesions occur with the greatest frequency in the mucosa of the colon and the lower few inches of the ileum, those in the colon being usually much more intense and extensive. The pseudo-membrane in case 6, however, is confined entirely to the small intestine, the ulcerations in case 32 are confined entirely to the small intestine, and case 27, although only a little of the ileum was affected, showed its most intense process there. Though the submucosa is at times affected there is no considerable change unless the mucosa has suffered severely. Only in the most intense inflammations does the muscular coat show participation in the process, and then very slightly, while the peritoneum escapes—case 4, with general peritonitis, being an exception.

As far as the other organs are concerned there were no characteristic findings. The mesenteric glands are usually somewhat enlarged, rarely markedly so, and grayish or pinkish. The lungs show hypostatic congestion and small areas of broncho-pneumonia unless the Shiga infection is secondary to some more pronounced pulmonary lesion. The liver is fatty in about the same percentage as in other infantile conditions. The spleen is, as a rule, unaffected, but when some other infection is added presents the characteristics common in all infectious diseases. The kidneys show, as a rule, cloudy swelling.

In eight cases cultures were made from all the organs at autopsy but never was the bacillus found except in the intestinal tract. The culture tubes—when tissues from the organs were transplanted in small quantity, except the lungs, where many different organisms were found, —either remained sterile or showed a growth of colon bacilli. In one case, streptococci were found in the liver. This negative bacteriological finding is the characteristic one in adults, though general blood infections have been reported. The method advised by Flexner, of plating considerable quantities of tissue, by which he was able to de-

monstrate the presence of bacilli in the liver and mesenteric glands, was not employed.

An examination for micro-organisms gives no very definite results. An innumerable host of bacteria, cocci and bacilli, are present in the pseudo-membrane and in the necrotic tissues; in the center of these masses they are about equally distributed, but one receives the impression that, in the tissues surrounding, the bacilli of the colon-typhoid morphology and staining properties predominate, but it is, of course, impossible to say that these are all Shiga bacilli. In the milder grades of inflammation the organisms of any kind are few in number, very superficially situated, with no particular type predominating. In this series the organisms invaded the submucosa in case 15 only.

In examining for bacteria in the sections my findings agree more nearly with those of Flexner,[3] who found in adults a general admixture of organisms on the surface of and in the mucosa, with a submucosa uninvaded, rather than with those of Strong and Musgrave, who found organisms not only in the mucosa but all through the areolar tissue, muscularis mucosæ and submucosa down to the muscular coat.

It is interesting at this time to compare somewhat in detail the pathological findings in these cases with those observed by Flexner,[3] and by Strong and Musgrave, in Manila,[4] the specific germ being the same. When we do this we find that only one of these groups (A) is comparable in any way with their Manila cases, though this bears many striking resemblances. There is a pseudo-membrane composed of necrotic tissue, emigrated and desquamated cells and myriads of bacteria. Flexner lays great stress on the fibrin in this pseudo-membrane, while Strong and Musgrave do not mention its presence. A moderate amount of fibrin was found in some, not all, of my cases. The submucosa is much affected, according to these observers, and this was my observation, and the changes were the same; but Flexner speaks of much fibrin formation in this coat as well as hemorrhages, the former of which Strong and Musgrave do not mention nor did I find fibrin or hemorrhages in this situation save in case 27, where hemorrhage continuous with that in the mucosa was found. Flexner says also that the submucosa may be affected with an intact or almost intact mucous membrane, while in my cases, when the submucosa participated in the process, it was only when the mucous membrane was greatly damaged. Case 3 is an exception to this rule, the submucosa being a little affected while the mucosa was practically normal. Flexner does not speak of, but Strong and Musgrave mention subacute cases with hyperplasia of the solitary follicles and superficial

erosions which suggest my group (B) with the follicular excavations. The other varieties that I have described find no prototypes in the published reports of Manila cases.

The foregoing report shows unmistakably that cases of Shiga bacillus infection exhibit most diverse pathological anatomy. The gross and microscopical changes of the extremes of these cases are so different that at first sight it would seem scarcely probable that they are caused by the same micro-organism. There are, indeed, many considerations which must be taken into account before a final opinion is passed upon the question as to what extent the lesions found are to be ascribed to the action of this bacillus.

It seems to me that in discussing this point, which is among the most important of all, we cannot afford to disregard the facts of clinical observation. A moment's reflection on the clinical course of the diarrheas of infants brings forcibly to our attention the common observation that some cases are extremely mild and respond almost immediately to ordinary therapeutic measures. In conformity with this fact it can be stated on the basis of my observations that a large percentage of fatal cases fails to show evidence of profound structural lesions. In view of the slight nature of these lesions the question arises as to what extent the infection is to be regarded as a cause of death in infants. As regards this question it may be said immediately that among these cases a certain percentage must be looked upon as intercurrent, or so-called terminal infections in children already debilitated by previous disease, whereas in the remainder the fact that the children were institutional children in a very depreciated state of health must be considered. It seems to me, therefore, that these slighter grades of infection in more vigorous infants are possibly the ones which respond so promptly to remedial measures.

In considering the severer lesions, particularly the ulcerative ones, the question immediately arises as to what extent the entire process is to be regarded as due to the Shiga bacillus. We are here confronted with the identical problem that has to be considered in dealing with similar infections in adults, and thus far it has not been possible to separate sharply the damage done by the Shiga bacillus and that which is subsequently done by the entire host of micro-organisms, pyogenic and others, normally contained in the intestinal tract. This much, however, may be said: The evidence favors the belief that the primary necrotic lesion is the result of the action of the bacillus of dysentery, the subsequent ulceration being brought about not improbably by the interaction of various micro-organisms and the ordinary

processes of demarcating inflammation. Beyond this point it does not seem possible to distinguish the action of the various micro-organisms in the intestine. The lesions in the intestine in children as in adults must for the present be conceived to be of two kinds; first, those due to the action of the dysentery bacillus, as already explained, and, second, of toxic products of this and perhaps other organisms, as is shown by the lesions of the submucosa and elsewhere. In this regard there is a uniformity in the conditions found in children and in adults.

It is important to take cognizance of the fact that, after all, in my cases the lesions found were not usually typical pseudomembranous inflammations; the pseudomembrane appeared either on the surface of ulcers or as isolated areas upon the mucous surface of the intestine. In this regard the changes in children seem to be in contrast to those thus far described in adults. But a still further distinction is found in the much more common involvement of the solitary and agminated lymphatic structures in children—the same structures in adults usually escaping.

If we endeavor to sum up the case as here made out for the Shiga bacillus we shall have to say that there are comprised under the lesions associated with it all grades and types of diarrheal disease, as distinguished by clinical symptoms and pathological findings, and that it can be affirmed that no particular type of such disease is distinguished from the others by a special etiological origin.

1. Centralblatt für Bact. u. Parasiten., 1898, XXIII, 599.
2. Deutsche Med. Wochen, 1901, XXVII, 784.
3. Middleton-Goldsmith Lecture, 1900.
4. Report of the Surgeon-General of the Army, 1900.
5. American Medicine, 1902, IV, 417.
6. The Journal of Medical Research, Vol. X, No. 1.
7. Martini und Lenz. Zeitschrift f. Hygiene u. Infectionkrank., 1902, XVI, 559.
8. Lenz. Ibid., 540.
9. Univ. of Penna. Medical Bulletin, Vol. XVI, Nos. 5-6.
10. The Journal of Medical Research, Vol. IX, No. 2.

A REPORT OF THE AGGLUTINATION REACTIONS OF THE BACILLUS DYSENTERIÆ WITH THE BLOOD SERUM OF INFANTS SUFFERING FROM DIARRHEA.

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(From the Thomas Wilson Sanitarium for Sick Children.)

The following summary is a record of the routine examination of the blood for agglutination with B. dysenteriae which was carried out at the Sanitarium during the summer of 1903. It does not, unfortunately, include all patients treated at the Sanitarium for in some instances blood was not obtained and, in others, the pressure of the usual clinical work prevented the examinations from being made.

The report is based upon the examination of 100 patients. The majority were studied once, but in a few instances two or more examinations were made. Forty-five cases yielded positive and fifty-five negative results. No result is recorded as positive unless the reaction occurred at a minimal dilution of 1 :100. When possible the dilutions in every case were carried up to 1 :1000 or farther.

The cases studied have been divided into groups according to the symptoms presented or the discovery, in cultures, of the bacillus of dysentery. For the present I am following the suggestions of Dr. Knox in denominating the cases in which the bacteriological findings were positive as "Dysenteria infantum." The other classes are those generally recognized. The following table expresses the results of the blood examination according to this view:

	Number of Cases.	Blood Examination.	
		Number Positive.	Number Negative.
"Dysenteria infantum"	40	26	14
Dyspeptic diarrhea and ileo-colitis	42	12	30
Dyspeptic diarrhea with malnutrition	4	2	2
Malnutrition and marasmus	11	5	6
Simple diarrhea	3	0	3
	100	45	55

This table is chiefly valuable in excluding the cases of simple diarrhea from the group of cases yielding positive reactions. Unfortunately the technical difficulties of dealing with stools in which the bacillus of dysentery is sought are still too great to permit of a classification of the disease being based upon the results of the bacteriological examinations. The general character of the agglutination reaction as regards the above more or less arbitrary grouping of the cases arouses suspicion immediately of the reliability of the cultural tests taken alone. As bearing on this statement the negative reactions which have been noted in cases from which the bacillus of dysentery had been isolated may be cited. Whether or not repeated testing of the blood might not have changed this result cannot, of course, be stated. An analytical study of the five cases of malnutrition and marasmus giving positive reactions yields the following data: Two cases had bloody stools in the spring; one gave a history of an intermittent diarrhea lasting two or three months, and one had a marked mucous diarrhea on entrance.

As regards the day of disease upon which a positive reaction was obtained the earliest ones were on the second day and third days —1:1000 dilution. Other early reactions were obtained on the 5th, 7th, 8th, and 9th days. Eight cases gave negative results on the 25th or 30th day: of these, two cases returning with relapse, were then positive.

The persistence of the reaction was found to be variable. One case positive on the 5th day was negative on the 31st day. Other cases were positive for longer periods. Two cases which had suffered from bloody diarrhea three months before admission to the sanitarium for malnutrition still gave reactions in 1:100 to 1:250 dilutions. Dysentery bacilli were isolated, at this time, by Bassett from both cases.

The limits of agglutination in 44 cases were as follows: 1:100, 13 cases; 1:250, 3 cases; 1:500, 5 cases; 1:1000, 22 cases; 1:1500, 1 case. In general it may be stated that the height of the reaction is in part determined by the degree of seeding of the suspension of bacteria—a light seeding often reacting higher than a heavier one. On the other hand, a quicker reaction could often be obtained with the heavier suspensions than with the lighter ones.

It is to be regretted that time was not allowed for working with the different types of the organism. All the tests were made with the Flexner-Harris bacillus although two strains of this bacillus were employed since it was found that a recent isolation from one of our cases gave more satisfactory results than the old stock cultures of the "Harris" organism isolated by Flexner in Manila. However, the choice

of this type of the bacillus for the tests was made on the basis of Gay's demonstration of the mannite fermenting properties of the organisms isolated the previous summer by Duval and Bassett; and this choice seemed to be justified by the fact that the dysentery bacillus isolated by Bassett during the past summer (1903) from the cases in the sanitarium, including those of this report, consisted entirely of this form of the bacillus.

The reactions were observed at one hour and at three hours, or in a few cases at four or five hour intervals. Of the positive cases 18 reacted in one hour and 26 at the later period. Some of the higher dilutions were disregarded at the second reading because of the multiplication and overgrowth of the bacilli.

Of the 44 positive cases 23 showed blood in the stools while at the sanitarium or gave a history of blood sometime during the illness. All cases except two showed mucus and a few cases pus in considerable quantity. Of the 42 cases in which blood was present in the stools, 24 gave positive agglutination reactions. Among the 18 negative cases were many of those tested early in the course of the disease.

DISCUSSION AND CONCLUSIONS.

SIMON FLEXNER, M.D.

The foregoing reports of an investigation into the bacteriology of the diarrheal diseases of children call for a word of discussion. Each report states with precision and in some detail the circumstances under which the task of investigation was conducted, from which an impression is immediately obtained of the strong bias under which the examinations were made. The purpose of the investigation was not, indeed, the renewed exhaustive study of the bacterial flora of the discharges of these children, but was the testing of the definite question of the presence and distribution of *Bacillus dysenteriae,* with which microörganism Duval and Bassett had the previous summer, while working under a grant from the Rockefeller Institute for Medical Research, associated in a causal relation certain of these diarrheal states. Since the supposed etiological significance of this pathogenic bacillus could best be tested further by an extensive study of the facts and conditions of its occurrence in different localities in children ill of diarrhea, the investigation was planned to accomplish this purpose.

In the carrying out of such a collective investigation it could not be expected that no external factors would enter to affect the agreement of the final results. Perhaps the factor that would operate chiefly in this respect is the relative experience of the different workers in dealing with the problems before them. I think myself fortunate in having been able to secure so large a number of bacteriologists who entered into the work assigned them with spirit, energy and determination; but I realized at the outset that the experience gained by certain of the workers at previous times in the very field which they were now to re-enter gave them great advantages over their colleagues who started upon the difficult task of separating the bacterial flora of the intestinal discharges after a few weeks of hurried preparation in its methods and in the special study of the bacillus of dysentery. Hence, in summing up the evidence for and against this microörganism as a possible cause of the diarrheal disease of children, in so far as the results of this investigation may be taken as affecting that evidence, account should be taken of the methods of its recovery which are, up to

the present, so imperfect that in the hands of one set of competent bacteriologists failure in 50 per cent. of the instances will occur, while the same methods in other and more specially instructed hands will yield successful isolation in practically every case in which it is sought. I draw attention to this discrepancy, while at the same time I am emphasizing the wide distribution of the bacillus established by these studies, for I conceive that both are arguments for a causative rôle which, while containing something of strength, contain also something of weakness.

That the character of the materials in which the bacillus is sought affects the result, all workers are agreed; but the experience of last summer (1903) has been convincing in showing that this factor is less important than the studies of Duval and Bassett seemed to indicate. And yet their view is still in part to be upheld, for in relative ease of recovery the particular kind of discharges with which they operated chiefly—those containing mucus and blood and fairly free of fecal matter—far exceeds the more common mixture of mucus and feces which constituted, in this study, the larger part of the morbid specimens examined. The mere presence of blood in the stools is of less moment than Duval and Bassett supposed; but feces or undigested food are when present distinct obstacles, apparently, to the isolation of the bacillus. Hence a second important factor which affects the general results to be considered in this review is the varied nature of the materials subjected by the different workers to bacteriological examination.

A third factor, and one of considerable moment, has to do with the manner of collection of the morbid material and the promptness with which it is distributed in the Petri plates. Just as feces and food make the isolation of the bacillus of dysentery more difficult by introducing into the plates a larger number of intestinal and extraneous bacteria, that in their turn either dilute the former organisms individually, or through their presence and products restrict the growth of the dysentery bacillus, so in the same manner do the extraneous bacteria of unclean napkins and parts interfere when present with its recovery. And as multiplication of the bacteria contained in the discharges continues outside the intestine, and fails to proceed equally in all kinds but more in one kind than another, it chances that the bacillus of dysentery, under these invidious conditions, is soon overgrown and rendered more difficult of isolation. Thus it happens that the circumstances under which the examinations were conducted,—the proximity or removal of the laboratory from the source of the specimens, the manner of collection of the latter, and the rapidity with which they

could be dealt with in the laboratory—will be found to have had a marked and unmistakable influence upon the individual results. To cite a case in point: Gay and Stanton's figures show that the material obtained from Bellevue Hospital under what are to be regarded as favorable conditions gave a percentage of successes almost 3 times as great as was obtained from the distinctly unfavorable specimens, for the purposes of this study, supplied from the tenement district in which none of the necessary precautions in collection could be carried out, and an unavoidably long interval of time elapsed between the passage and the making of the plates at the laboratory. In keeping with this discrepancy is the fact that the plates of the one series (Bellevue) were practically free from extraneous bacteria while those from the other series (tenement district) were often grossly contaminated.

There can be no doubt that the discharges do not as a rule contain the bacilli of dysentery in such numbers or combinations as make possible their recovery as readily or in as large numbers as from the intestinal mucosa. I drew attention to this fact on the basis of my studies of acute tropical dysentery (Manila), and it has been confirmed by the studies of Vedder and Duval upon institutional dysentery in this country as well as by Duval and Bassett in their study of children in 1902. A further confirmation is found in the foregoing reports of Bassett and of Wollstein and Dewey. It is of interest to note that gentle scraping of the rectal mucosa during life will yield material from which the dysentery bacillus may be recovered when it has not been isolated from the natural intestinal discharges, and the most constant results are obtained from deeper scrapings of the mucosa of the intestine *post mortem,* the autopsy having been made soon after death.

This intimate relationship of the bacillus of dysentery to the substance of the mucosa of the intestine, in which locality, under pathological conditions, at least, it seems easily able to survive and multiply, is of considerable significance; and the reverse fact which teaches that this organism increases far less readily and is quickly overgrown in discharges when once outside the body, can be interpreted as indicating that it is less well adapted for a saprophytic than for a parasitic existence. The bearing which these data must have upon our views of the pathogenic properties of the bacillus of dysentery need not be especially emphasized.

In the course of the investigation carried on during the summer, 412 cases of diarrheal disease among children were studied bacteriologically with reference to the presence of the bacillus of dysentery. Of this

number positive results were obtained in 279 or in 63.2 per cent. of all cases examined. Since these figures are made up from the totals of all the reports a glance at the following table will show the manner in which they have been secured. And when it is remembered that the cases studied were not as a rule selected but taken as they entered hospitals and dispensaries, the prevalence of the bacillus of dysentery in children is no less than remarkable.

Investigator.	Number of Cases Studied.	B. Dysenteriæ Present.		B. Dysenteriæ Absent.	
		Number of Cases.	Per cent.	Number of Cases.	Per cent.
Duval and Shorer	79	75	94.	4	6.
Bassett	73	51	70.	22	30.
Wollstein and Dewey	62	48	78.	14	22.
Cordes	51	26	51.	25	49.
Waite	47	19	40.	28	60.
Kendall	31	29	93.5	2	6.5
Lewis	21	11	52.5	10	47.5
Gay and Stanton, Bellevue Hospital	20	13	65.	7	35.
Gay and Stanton, Tenement District	28	7	25.	21	75.
Total	412	279	63.2	133	36.8

If we turn our attention now to the character of the discharges used in the investigation we will be struck with the great preponderance of mucus and fecal specimens over those in which blood and mucus were contained:

Investigators.	Total Number of Stools Reported.	Blood and Mucus.*	Mucus.	Mucus and Feces.	Feces Alone.
Duval and Shorer	79	25	15	36	3 (?)
Bassett	64	26	19	17	2 (?)
Wollstein and Dewey	60	20	0	40	
Cordes	51	9	0	33	9
Gay and Stanton	48	12	1	35	
Waite	43	16	0	26	1
Kendall	31	5	1	25	
Lewis	21	7	0	14	
Total	397	120	36	226	15

* With or without feces.

Thus of 397 specimens of intestinal discharges reported considerably less than one-third contained blood in quantities appreciable to the naked eye. This table is by itself incomplete, for what is required before any conclusions can be drawn of the relation of the character of the discharges to the occurrence of Bacillus dysenteriae is the relative proportion of the stools of different kinds which were associated with the organism as proven by cultural tests. The next table has been prepared to express this association and gives the exact figures as far as they can be gathered from the reports.

Investigators.	Total Number of Positive Results from Stools.	Blood and Mucus.	Mucus.	Mucus and Feces.	Feces.
Duval and Shorer....	74	21	13	38	2 (?)
Bassett.....	43	19	10	14	0
Wollstein and Dewey..	46	17	0	29	0
Cordes.....	26	6	0	18	2 (1?)
Gay and Stanton.....	20	6	1	13	0
Waite.....	16	9	0	7	0
Kendall.....	29	5	1	23	0
Lewis.....	11	5	0	6	0
Total.....	265	88	25	148	4

This table confirms the preceding one since it exhibits that the proportion of specimens containing visible blood and constituting so-called "positive" discharges is about one-third of the whole number yielding in culture Bacillus dysenteriae, and it further bears out the statement made in the early parts of this review, namely, that the larger part of the specimens from which the bacillus of dysentery was isolated were not admixed with blood. In view of this finding it could be predicted that the muco-fecal stools would head the list of instances of successful recovery; and it is also important to observe what has hitherto been overlooked, that in at least three instances (one example doubtful—probably feces diluted with serum) the bacillus of dysentery was secured from fecal material in which neither blood nor mucus was detected.

It is not my intention to discuss the bearing of these facts and findings upon the clinical types of the diarrheal diseases of children. Fortunately many of the cases were carefully observed by clinicians whose records will serve the purpose of correlating the results of the bacteriological examinations with the clinical features presented by the children. This part of the present investigation will be dealt with in another portion of this publication.

When we stop to consider the wide distribution in children of the bacillus of dysentery, which is proved by this study, the question of the natural habitat of the organism and its mode of entrance into the body arises in our minds. Unfortunately our knowledge upon the habitat of the bacillus is practically nil. The bacillus has not yet been found in our surroundings and is known only as occurring in the intestine and very rarely elsewhere in human beings. The facts with reference to its pathogenicity, as they appear from the investigations of outbreaks of bacillary dysentery in adults, would lead us to suppose that it led a parasitic existence in the body of human beings and was scarcely to be sought among the saprophytes of the intestine. But the broader fact that the organism occurs in children who may be very little ill compels us to examine more carefully and openly into the assumption of a purely parasitic existence, which we have hitherto and perhaps tacitly made in regard to the dysentery bacillus.

It has of course occurred to all investigators of the pathological conditions supposed to be due to the dysentery bacillus to search for the organism in healthy persons. Shiga, Flexner, Kruse, Duval and Bassett and Wollstein have in turn sought the organism in the discharges of healthy adults or children unsuccessfully. But the experiences of the past summer called for renewed and painstaking investigations of this question, and hence, at my request, Dr. Wollstein and Dr. Duval attacked it afresh. At Dr. Welch's suggestion I had Dr. Duval search for the organism in infants to whom mild cathartics had been administered with the result that he isolated it in very small numbers from the stools of two healthy, milk-fed children. The few colonies obtained gave the reactions of the "Flexner-Harris" bacillus.

I do not intend to dwell long on this finding which calls, I think, for confirmation from a wide and varied material drawn from human beings in health and, perhaps, in other intestinal diseases than those in which the organism has now been found. That the diarrheal diseases of a definitely foreign and specific origin, *e.g.*, tuberculosis, may not yield the bacillus of dysentery even after prolonged search is indicated by Kendall's report upon two instances of tuberculous enteritis.

The unexpected finding of the bacillus of dysentery in healthy infants and the wide occurrence of that organism in the common form of diarrhea in children, open up a considerable field of speculation upon the real pathological significance of the organism. It would seem as if we had no grounds for denying it, in many pathological cases, significance; for the presence of the agglutination-reaction, the increasing number of the organisms in the discharges and their close relationship

to the intestinal mucosa in such cases afford ample proof of its pathogenic action. Since these data have been considered convincing with reference to adult-infections they will hardly be denied application in the cases of the children we are now considering.

A point of difference in the mode of spread of the adult and children infections is at first sight apparent. While the former often extend with epidemic severity, the latter do not present the features of spreading epidemic infections. The cases of infection in children seem to be examples of individual inoculation, although occasional examples of contagion—from child to child—occur as in the instance recorded by Bassett. However, the corresponding occurrence of sporadic infection among adults is also established as in the cases studied in this country by Vedder and Duval and later by Gay and Duval. And, moreover, the endemic bacillary dysentery of the tropics which does not flourish as an epidemic disease but as an individualistic one arising from a common source, presents some of the striking epidemiological characters of the infections in children that we are discussing.

When we turn our attention to the probable source of the infecting bacillus in children we appreciate immediately our entire ignorance of the habitat in nature of the organism. Whether it gains access to the intestinal tract with milk, water or other substances we can only conjecture. But it is among the possibilities that the bacillus of dysentery is, after all, an occasional—perhaps a constant?—inhabitant in some districts of the intestinal canal where it survives saprophytically among the other intestinal bacteria. If such a possibility be admitted then it might also be considered whether a whole host of *insults* to the intestinal mucosa or functions may not allow the less restrained growth of the organism and eventually the acquisition of parasitic and invasive properties which could lead to more or less serious pathological disturbances.

In bringing forward this speculation I am not unmindful of its bearing upon our knowledge of those endemic and epidemic infections in which there can, I think, be no doubt of the importation from without of a highly pathogenic organism preceding the outbreak of symptoms. That two modes of infection may occur—auto-infection and extra-infection—is not inconsistent with our knowledge of other diseases. I need only refer to the lobar pneumonias in which the abiding micrococcus lanceolatus of the saliva may be the exciting cause or as in house and institutional epidemics of that disease, a more intensely pathogenic organism taken into the body from surrounding persons or things may be the direct source of contagion. I shall not pursue

this line of argument further; and I mean to content myself with the observation that we must be willing to admit for the bacillus of dysentery, what we have come to admit for many other pathogenic species of microörganisms,—*e.g.*, cholera bacilli, tubercle bacilli, pneumococci, diphtheria bacilli and pus cocci—namely, the influence of other factors than the mere presence of the injurious bacillus in determining the origin of infection. That the bacillus of dysentery has a wide distribution in children may be taken as established by this investigation; but whether in every instance in which it has been found it is to be considered as acting in a pathogenic manner and hence is to be regarded as the prime or even proximate cause of all existing intestinal lesions, are questions to which final answers are not yet to be given.

It is not without theoretical, perhaps not without practical interest, that the type of bacillus which prevails in children is that obtained by Flexner from certain cases of Philippine dysentery. This "Flexner-Harris" type of the organism was found in the great majority of all the children from whom dysentery bacilli were isolated, and in the experience of certain of the investigators was the only type met with. A statement of the figures will best exhibit the comparative frequency of prevalence of the two types:

Investigators.	Total Number of Cases Yielding B. Dysenteriæ.	Number Yielding "Shiga" Type Alone.	Number Yielding "Shiga" and "Flexner-Harris" Types.
Duval and Shorer	75	11	6
Kendall	29	4	0
Lewis	11	3	0
Waite	19	2	0
Gay and Stanton	20	2	0
Cordes	26	1	0
Wollstein and Dewey	48	0	0
Bassett	51	0	0

Since the cases of the "Shiga" type of infection are so unusual, it will be worth while to examine the records in order to determine whether they present any features which may be regarded as peculiar. It may add to the clearness of the matter to speak of the cases as consisting of "single" and "double" infections. Thus we shall have single infections with the "Flexner-Harris" or "Shiga" type of bacillus or double infections in which both types are associated. The following table shows the number of "Shiga" bacilli obtained from the plates and their relation to the associated "Flexner-Harris" type, as well as the nature of the discharges yielding them.

Number of Case.	Investigator.	Total Number of Colonies Transplanted from Plates.	Number of Colonies of "Shiga" Type.	Number of Colonies of "Flexner-Harris" type.	Description of Material Yielding "Shiga" Type. S. = Stool.
7	Duval and Shorer	Not stated	2	?	S. Mucus and feces; brown semi-solid.
8	Duval and Shorer	Not stated	1	7	S. Yellow mucus.
11	Duval and Shorer	Not stated	2	5	S. Muco-fecal.
13	Duval and Shorer	Not stated	28	2*	S. Green muco-fecal; little blood.
15	Duval and Shorer	Not stated	1	0	S. Blood-flecked mucus.
17	Duval and Shorer	Not stated	1	0	S. Green, muco-fecal; blood-flecked.
19	Duval and Shorer	Not stated	3	1	S. Small, bloody mucous.
33	Duval and Shorer	Not stated	34	0	S. Large, fluid; muco-fecal.
36	Duval and Shorer	Not stated	3	0	S. Large, liquid; muco-fecal.
38	Duval and Shorer	Not stated	2	4	S. Green, muco-purulent.
43	Duval and Shorer	Not stated	45	0	S. Yellow mucus.
55	Duval and Shorer	Not stated	4	0	S. Curds and muco-feces.
56	Duval and Shorer	Not stated	2	0	S. Green; muco-fecal.
66	Duval and Shorer	Not stated	1	0	S. Blood and mucus.
68	Duval and Shorer	Not stated	1	0	S. Mucus and blood flecks.
73	Duval and Shorer	Not stated	1	0	S. Blood-flecked mucus.
76	Duval and Shorer	Not stated	8	0	S. Green; muco-fecal.
1	Kendall	Not stated	Not stated	0	S. Green-yeliow; blood-flecked.
2	Kendall	Not stated	Not stated	0	S. Green-yellow fluid.
3	Kendall	Not stated	Not stated	0	S. Green-yellow fluid.
34	Kendall	Not stated	Not stated	0	S. Green-yellow, semi-solid; mod. mucus.
2	Lewis	Not stated	11	0	S. Large, curdy; mucus and feces; blood flecks.
7	Lewis	Not stated	14	0	S. Much mucus, some feces.
19	Lewis	Not stated	10	0	S. Large; muco-fecal.
44	Gay and Stanton	Not stated	2	0	S. Small quantity; mucus and blood.
45	Gay and Stanton	Not stated	8	0	S. Greenish-yellow; mucus and feces.
35	Cordes	22	2	0	S. Soft, yellow and brown; little mucus.
21	Waite	17	1	0	Rectal tube; thin, mucus and blood.
41	Waite	70	2	0	S. Pasty, dried; blood-flecked.

* Mixed "Flexner-Harris" and "Y" type of bacillus. Vide infra.

Scrutiny of the table brings out the absence of any strikingly peculiar behavior of the "Shiga" type of bacillus in the plates and shows that what is true in respect to the numerical occurrence for one type is equally true for the other type. For the most part the number of colonies of the "Shiga" bacillus isolated was small, although in some instances it was fairly large. It may be of interest to note the rare occurrence of double infections and the preponderance of the "Shiga" organism in the examples of this form of infection.

The table also exhibits the entire absence of qualities in the discharges, that would serve to characterize this group of cases as peculiar or different from the general cases in which the "Flexner-Har-

ris" type of bacillus occurs alone. And I am not aware that the group of cases yielding the "Shiga" type of bacillus presented distinctive clinical features. Consequently we must, for the present, look upon the two groups of cases, namely the one in which the "Flexner-Harris" type of bacillus and the other in which the "Shiga" type has been found, as of equal value in regard to the part played in them by the bacillus of dysentery.

In order that no misapprehension of the results may occur I should state that all the investigators were on the alert to discover cases in which the "Shiga" type of bacillus was present. The desirability of determining the types of all colonies of the dysentery bacillus obtained was impressed upon the workers, and as each report deals with the matter of types it is fair to asume that no "Shiga" colonies were overlooked by accident or through omission of the tests.

Our present knowledge of the bacillus of dysentery has led us to distinguish two related types of bacilli to which the designations already given have been applied. But it is not only probable, but indeed proven, that by the employment of additional physiological tests other variations in behavior of bacilli of this general kind may be detected. An interesting variation of this nature has been described by Hiss and Russell in their bacillus "Y." This bacillus while exhibiting the general biological qualities of the "Flexner-Harris" organism differs from the latter in failing to attack dextrine with the production of acid. In only one set of the studies of the summer was attention paid to the occurrence of the last named organism. At the suggestion of Dr. Hiss, Duval and Shorer tested all the "Flexner-Harris" bacilli, so-called, which they isolated from cultures, upon dextrine and found, in this way, bacillus "Y" twelve times. With one exception in all 12 instances the organism was associated with the "Flexner-Harris" bacillus. It is of some interest to note that its numerical relations to the "Flexner-Harris" bacillus were as indefinite as was the case with the "Shiga" type of organism; for while in some instances it formed only a fraction of all the colonies of B. dysenteriae recovered from the plates in others it was the predominating organism.

If we pause for a moment in order to recapitulate the types of bacilli which are now admitted to belong to the group of B. dysenteriae and to consider the physiological properties upon which distinction is based the following data will be obtained:

(1) "Shiga" type: attacks glucose, without action on other sugars including mannite and lactose.

(2) "Flexner-Harris" type: attacks glucose, mannite and dextrine; does not attack lactose.

(3) Bacillus "Y" (Hiss and Russell), attacks glucose and mannite; no action on dextrine and lactose.

In the course of the collective investigations of the past summer another bacillus was met with by several of the workers which, should it prove to belong to this group of organisms, will constitute, so far as physiological properties are concerned, another variation. The properties of this bacillus are described in some detail by Duval and Shorer although its occurrence is noted also by Gay and Stanton and Kendall. Duval and Shorer state that in two cases a bacillus was secured which agreed morphologically, in staining properties, and in the usual cultures with a typical control culture of B. dysenteriae and, in addition, that it agglutinated in considerable dilution with antidysenteric serum from the horse. On the other hand, its action upon milk and upon lactose-serum-water distinguished it from the types of dysentery bacilli now recognized. The bacilli in question cause first an acidity of the milk which reaches its height in (*circa*) 48 hours, after which there is a gradual return to alkalinity. In this respect the bacillus resembles the usual cultures of B. dysenteriae. But after a second period of 5 to 6 days acidity again makes its appearance, exceeds in intensity the primary reaction, and is permanent. That the second acidity arises from action upon lactose is shown by the coagulation by the bacillus of Hiss' serum-water to which pure lactose has been added. Reference to the epitomized statement given above, of the effect of at least three "types" of dysentery bacilli upon several kinds of sugar, will at once make clear this distinction as none of these attacks lactose.

In view of the variations in physiological properties which we are discussing it is worth pointing out that Duval and Shorer have separated further this anonymous bacillus into two forms of which one attacks and the other is without action upon dextrin. In other words the same physiological differences exhibited by the "Flexner-Harris" bacillus and "Bacillus Y" are displayed by the two forms of the bacillus forming acid on lactose. In order then to complete our statement of this group of organisms including the still doubtful bacilli which act on lactose the following series is required:

(1) "Shiga" type: attacks glucose; without action on other sugars including mannite and lactose.

(2) "Flexner-Harris" type: attacks glucose, mannite and dextrine; does not attack lactose.

(3) "Bacillus Y": attacks glucose and mannite; no action on dextrine and lactose.

(4) Duval and Shorer "Bacillus A": attacks glucose, mannite and lactose; no action on dextrine.

(5) Duval and Shorer "Bacillus B": attacks glucose, mannite, dextrine and lactose.

The manner in which this group of organisms agrees and differs is of interest and importance, and cannot fail to arouse the suspicion that their physiological properties are, at present, in a very unstable condition. We are therefore warned, as it were, away from any attempt to employ the physiological activities alone as bases of subdivisions of the entire family—if family it be—of the dysentery bacilli. And it is self-evident that the future study of the bacilli of the Shiga class—so-called—must be conducted with greater delicacy and precision than in the past in order that the extent of the variations which the class presents may be ascertained with accuracy.

Besides the last considered bacilli which have a strong resemblance to the bacillus of dysentery, Wollstein and Dewey, Kendall, and Duval and Shorer have encountered another bacillus which agrees with that organism in some qualities but which is probably entirely distinct from it. The chief cultural peculiarity of this unidentified bacillus is its strong alkali formation in litmus-milk. Duval and Shorer give the fullest description of the organism from which the following is abstracted: The bacillus possesses morphological and staining properties which do not distinguish it from the "Shiga" type of B. dysenteriae. In cultures upon the ordinary fluid and solid nutrient media it is also indistinguishable. The agglutinations with horses' anti-dysenteric serum is positive up to 1:500 to 1:1000. On the other hand, litmus-milk and semi-solid jelly (Hiss) serve to bring out striking differences. The former shows a primary acidity, after which an amphoteric and then alkaline reaction appears. But the last instead of remaining moderate goes on to strong alkalinity, the milk assuming at times a blue-black color. With some of the early isolations the milk underwent peptonization; but this proteolytic power the bacillus loses in subcultures. The semi-solid jelly often establishes rapidly a distinction in that a part of the bacilli of this kind are sufficiently motile to cloud the medium. But as a certain number of the cultures are either non-motile or very feebly motile, the milk medium must be resorted to for differentiation—a process requiring some days. As these bacilli do not attack the sugars, except dextrose, the serum-water medium is not useful for purposes of differentiation (distinction from B. fecalis

alkaligenes). Two rabbits were immunized to cultures of the "alkaline" bacilli. The serum of these animals was positively agglutinative 1 :20,000 with the bacilli used for inoculation and 1 :25 to 1 :50 with dysentery bacilli. The exact position of this organism is left unestablished, but it probably is entirely distinct from the group of B. dysenteriae.

One of the immediately suggestive facts brought out by the tables in the foregoing reports is the great variation in numbers of dysentery bacilli isolated from the cases. When one glances through the tables and observes examples yielding 1, 2, 3 or a half-dozen colonies of the bacillus he must be impressed with the narrow line which separates "positive" from "negative" examinations; besides which he may be led to wonder whether an organism which occurs in such small numbers as these figures indicate can have any specific relation to pathological states of the intestine. The latter question has already been referred to in this discussion, but it is desirable to add a word upon the former one.

In the course of the summer's work I became convinced that the isolation of the dysentery bacillus from difficult stools was often determined by incessant vigilance and the transplantation of very large numbers of colonies to glucose-agar or the semi-solid jelly. Since the colony-form is only roughly useful in selecting favorable colonies it becomes essential to transfer to one of these media every suspicious colony arising on the plates; and thus several score of failures may at last be crowned with one or more successful tubes. It is unnecessary to add that even this costly method does not serve entirely to avert failure.

On the other hand, the statement of the recovery of larger numbers of colonies—30, 50, etc.—does not indicate the entire or even relative richness of the plates in dysentery bacilli, for this number may have been obtained in one or two pickings from a few plates, after which no further search was made. That the bacillus may occur in much larger numbers and even exceed the other intestinal bacteria is shown by those cases (reported by Duval and Shorer) in which the dysentery bacilli were present either alone or in such overwhelming numbers as to suppress entirely the growth of the colon bacilli.

I have entered into a consideration of the facts of the numerical relation of the bacilli to show that I have not overlooked their bearing upon the pathogenic properties of the organism and to emphasize, more especially, the imperfection in our methods of isolating the bacillus from dejecta. For it is, I think, highly probable that only rarely and

under unusual circumstances are the conditions so favorable as to yield to our present methods the organisms in large numbers. And hence the prediction can be ventured that some other procedure, possibly one of enrichment analogous to that used in isolating the comma bacillus from choleraic discharges, will yield far more constant and unambiguous results. Indeed, Shiga having appreciated, apparetnly, this difficulty has devised a method of enrichment, but unfortunately it is too complex and initially difficult, in its present form, for application to routine work.

It is perhaps unfortunate that more attention was not paid to the agglutination of the dysentery bacilli and possibly other bacteria growing upon the plates by the blood of the patients. The concentration of the work into the few hot summer weeks, during which the great majority of the cases arise, and the detailed nature of the cultural studies rendered the systematic investigation of the agglutination-value of the blood impractical. Besides this, it was soon discovered that to obtain even the small quantity of blood needed for the test so prejudiced the mothers in dispensary and tenement-district practice that they became obstinate and often declined treatment. The circumstances were different in hospital practice and consequently Bassett's records, which are based upon fuller studies by Winne, and Wollstein's and Dewey's and Cordes' results are of reliability and value. It is to be hoped that Dr. Winne will publish his figures in detail; but the data given in the several reports exhibit the high degree of agglutinability which may be acquired by the blood, as well as the uncertainty of the agglutination-test as an index of the presence of B. dysenteriae in the intestine or discharges. The original studies on agglutination made by Duval and Bassett and the subsequent ones made by Wollstein are borne out by these later results. That the reaction may persist in the blood for some weeks after health has been re-established is shown by several intances given in Bassett's report.

Conclusions.

1. The Bacillus dysenteriae can be isolated from the intestinal discharges and the intestinal mucosa of a large percentage of children suffering from the diarrheal diseases prevailing along the Atlantic sea-board of the United States during the summer months.

2. The Bacillus dysenteriae is to be sought especially in the mucus thrown off by the intestinal mucosa in these diseases and in the substance of the mucous membrane itself. The bacillus exists in smaller

numbers in, or is recovered with far greater difficulty from, the fecal matter that often is admixed with the mucus.

3. Blood admixture makes the isolation of the bacillus of dysentery from the intestinal discharges more readily accomplished, as it generally indicates infections of severer grade; but the mere presence of blood is of less moment than the occurrence of mucus, since it is in the latter material that the bacillus of dysentery resides.

4. The number of colonies of Bacillus dysenteriae recoverable in cultures is in a general way indicative of the severity of the lesions and symptoms of the disease. Some cases, however, of marked severity yield few colonies and others of marked mildness a larger number of colonies of the bacillus.

5. The total number of colonies of Bacillus dysenteriae obtainable is, as a rule, far below the number of colonies of the usual intestinal bacteria which develop upon the plates; but in a very few instances the number of colonies of the dysentery bacillus equals or exceeds that of all other organisms, and in exceptional specimens the bacillus alone appears in the cultures.

6. The type of Bacillus dysenteriae which preponderated in the children is the so-called "Flexner-Harris" organism. The "Shiga" type of the organism is exceptionally met with, and occasionally both types are found in association.

7. Types of Bacillus dysenteriae of less well-established properties have also been encountered. Among these are Bacillus "Y" of Hiss and Russell and another distinct type which demands additional study before admission to the group, whose special property is its power to act upon lactose with acid production.

8. The blood of the children suffering from diarrheal disease agglutinates at times the bacillus of dysentery in high dilutions; but this agglutination by the blood does not proceed hand in hand with the occurrence of the bacillus in the intestine. The agglutination reaction is not to be treated as an index of the presence of, or infection with, Bacillus dysenteriae.

9. The close association of Bacillus dysenteriae with the intestinal mucosa, and the increased numbers of the organism found under definite pathological conditions, the established pathogenic action of the bacillus for human beings, and the specific blood changes met with in many of the cases of diarrheal disease, all speak for a relationship of cause and effect between the bacillus of dysentery and the lesions of the intestine.

10. It is probable although it is not proven that Bacillus dysenteriae

appears, at times, among the saprophytic bacteria of the contents of the intestine. The frequency of its isolation in all grades of diarrheal disease in children would be in conformity with the view of such a saprophytic existence and the acquisition, under pathological conditions, of pathogenic and invasive properties.

11. Should it be established that Bacillus dysenteriae is occasionally or regularly to be found among the bacteria of the cavity of the intestine, the dangers of the entrance from without of specially pathogenic examples of the organism are not to be disregarded. The contagiousness of bacillary dysentery among adults, and the rarer instances of diarrheal contagion among children, prove the necessity of recognizing such an extra-infectious origin of the disease.

12. Streptococci in large numbers are found frequently associated in cultures with Bacillus dysenteriae. Both organisms survive side by side and would seem not mutually to inhibit each other's development. What part is to be ascribed to each in the production of the lesions of the intestine and the symptoms of disease is not established by this investigation. Nor is the possible action of any other of the many bacteria of the discharges excluded by the special findings of the investigation.

13. The central fact brought out by this collective investigation is the frequent occurrence in the diarrheal diseases of children of a specific micro-organism, which hitherto has been held to be of special pathogenic action in human beings, and to be the cause of that form of dysentery among adults and also among children, which is characterized by necrotic and pseudo-membranous lesions of the intestine and marked infectiousness.

14. The lesions of the intestines observed in the children who have succumbed to the diarrheal diseases treated of in this publication have been very varied in character; but there has rarely been found among them the particular kinds of pathological changes which characterize pseudo-membranous entero-colitis.

A CLINICAL STUDY OF SIXTY-TWO CASES OF INTESTINAL INFECTION WITH THE BACILLUS DYSENTERIÆ (SHIGA) IN INFANTS.

BY

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The cases that make up the material for this study were all observed by the writers at the Vanderbilt Clinic during the months of July, August and September, 1903. The patients were brought to the dispensary, which is an outpatient service, and the milder cases were seen only every alternate day. The severer cases were in addition visited and treated at their homes on the days that they did not come to the clinic by Drs. Peter Irving and Frank Erdwurm, whose efficient cooperation made full reports possible. To insure uniform records use was made of printed blanks upon which could be recorded the history, physical examinations and daily observations of each case.

When a child was brought with a history of diarrhea, effort was made at the time of the first visit to obtain a fresh stool for immediate bacteriological examination. By using the thermometer by rectum or inserting a suppository it was possible in most cases to obtain a stool. The stool was passed into a sterile piece of unbleached cotton, then taken at once to the bacteriologists, Duval and Shorer, working in the same building. In forty-eight hours a bacteriological report on the presence or absence of the dysentery bacillus could be obtained.

At first only those cases were examined bacteriologically that gave the history or presented symptoms of a moderately severe diarrhea;

but later, on account of the numerous positive findings, all cases of mild diarrhea and intestinal indigestion were also examined.

This makes our report of far greater interest, our cases being successive ones, no selection at all having been attempted after the first 4 cases, while other cases that have been published up to this time have been those selected for their severity or for some reason regarded as suitable and likely to contain the bacillus of dysentery. One small series examined seriatim has been reported.

Some patients were seen but once; in others, though seen several times, the result of the disease was unknown. Undoubtedly some of these cases recovered so that they were not brought back to the clinic; others refused to return after the first injection of the serum.

As routine measures, cow's milk was immediately discontinued and not resumed for several days; in breast-fed infants the nursing was forbidden for a time. Barley water, rice water or broth was substituted for the milk. Free catharsis was obtained by means of calomel and castor oil. Other drugs were rarely used.

There were in all 62 cases of infection with the *Bacillus dysenteriæ* (Shiga); of these 2 were observed during June, 33 in July, 18 in August and 9 in September. The investigation was begun late in June and ended September 15th, so that only during July and August were observations carried throughout the whole of the month; hence the small number of cases reported in the first and last months, June and September, has little significance.

Age.—Eight of the patients were under 3 months; 14 were between 3 and 6 months; 15 were between 6 and 9 months; 9 were between 9 and 12 months and 15 were over one year, and of 1 the age was not stated.

Of the 8 patients under 3 months of age, 5 were only slightly sick, 1 moderately and 2 severely sick.

Of the 14 patients between 3 and 6 months 7 were mild infections; 4 moderately severe; 2 severe, and 1 patient was seen only once.

Of the 15 patients between 6 and 9 months 3 were mild cases; 9 were moderately severe, and 3 severe.

Of the 9 between 9 and 12 months 5 were moderately severe and 4 severe cases.

Of the 15 over 12 months, 1 was a mild case, 11 were moderate cases and 3 severe cases.

From an analysis of these cases it would appear that the number of moderately severe and severe cases increases proportionately with the increase in age. This is explained, however, by the fact that a

majority of the mild cases under 6 months of age in this series were breast-fed.

Previous Illness.—An attempt was made to learn if the patient had previously suffered from diarrhea and by reason of this was more susceptible to infection with the *Bacillus dysenteriæ.* The statements were so unreliable that no conclusions could be drawn. No other predisposing cause in the way of disease could be discovered.

Character of Food.—Of the 14 severe cases, 1 was breast-fed, 5 were given condensed milk, 2 Straus' sterilized milk, 2 grocer's milk, 3 fairly clean bottled milk, and 1 case not stated.

There were 14 children entirely breast-fed; 2 children were partly breast-fed; 11 children had been fed on grocery milk; 7 on bottled milk of fair quality; 8 were fed partly or wholly on sweetened or unsweetened condensed milk; 5 on proprietary foods without milk; 2 on Straus' sterilized milk; 2 on home sterilized milk; 1 on peptonized milk; 4 on general diet and no statement in regard to 7.

Length of Symptoms before Observation:

Symptoms	had	existed	for	1 day	in	5 cases
"	"	"	"	2 days	in	7 "
"	"	"	"	3 "	in	8 "
"	"	"	"	4 "	in	5 "
"	"	"	"	5-10 days	in	17 "
"	"	"	"	11-14 "	in	7 "
"	"	"	"	1-3 months	in	10 "
				No statement	in	3 "

Forty of the cases had given symptoms for one week or less showing that they were brought while they were still acutely ill.

Length of Time under Observation:

1-3 days	28
4-7 days	12
8-14 days	10
2 weeks and over	8
No record (seen only once)	4

Condition at the Beginning of Attack.—Of the 62 cases whose condition at the beginning of the attack was noted, 31 were well nourished; 2 fairly nourished; 11 poorly nourished; 13 were emaciated, weak and in wretched condition; 2 were in collapse and practically moribund on the first examination.

It is most interesting and instructive to notice in this connection that of the 31 children who were well nourished, 14 had a very mild form of disease, 12 were moderately ill and only 5 severely ill; of

the 2 fairly nourished, 1 was very slightly and the other severely ill; of the 11 poorly nourished, 7 were moderately, 3 severely and only 1 slightly ill. Of the 13 emaciated, 3 were severely ill, 10 moderately and not one had the disease in a mild form. From this it would seem that the most important factor in determining the character and severity of the disease is the previous condition of the child.

Of the cases observed by us 16 were very mild, 31 were moderately severe and 14 were severe; 1 case was lost sight of and so was unclassified. We characterized as mild those cases that had more frequent passages than normal, but not more than 10 a day, with a temperature of less than 100.5° F. These stools contained undigested food, usually mucus but no blood (such cases were not really sick). Those cases were classified as moderate that had a temperature over 100.5° F. or had frequent passages containing mucus and, sometimes, a slight amount of blood. These cases were really sick and showed constitutional symptoms. The severe cases comprised those having marked constitutional symptoms and great depression with frequent mucous stools, often with much blood; and, while the temperature of these cases was usually considerably elevated, many of them and some of the most severe ran an almost afebrile course.

Thirty-four cases did not show a temperature of over 100.5° F. and thus more than one-half of those seen by us were practically without fever. Vomiting occurred in 19 cases, usually at the beginning of the attack.

The number of stools in 24 hours was from 2 to 5 in 5 cases
" " " " " " " " " 5 to 10 in 35 cases
" " " " " " " " over 10 in 20 cases.
In 2 cases not stated.

Two cases had stools without any mucus; mucus was present in all other cases in varying quantity from a minute amount to practically the whole stool. Blood was present in 17 cases; the quantity of blood varied from a few streaks to enough to color all the mucus; no clots of blood were ever observed.

The following cases are cited as representing types of the different degrees of severity:

Mild. (Breast-fed infant) P. B., 5 months old, nursed entirely, every 3 hours. Had never been ill and his condition at the beginning of the attack was good. His illness began two days previously with 3 green mucous stools a day. No fever, no vomiting, no blood in the stools. Physical examination was negative. He was rather restless but otherwise seemed perfectly well and had a temperature of only 100° F. The stool seen at the dispensary was green, mod-

erately large, semi-liquid with mucus, no blood. Breast-feeding was ordered discontinued and barley water feedings substituted; small doses of calomel were given. The following day the condition was the same, character of stools unchanged and the same number. The third day the stools were 2 in number, yellow, fecal, with only a little mucus and everything seemed so satisfactory that breast feeding was resumed with an absolutely uninterrupted convalescence.

Such a case would formerly have been considered a very mild case of intestinal indigestion; but the bacteriological examination showed the presence of the "Flexner-Harris" or acid producing type of dysentery organism.

Mild. (Bottle-fed infant) W. P., 6 months old, in good general condition. Never had the breast, bottle-fed from birth; at onset was being fed a mixture of malted milk 3 teaspoonfuls, and water 1 pint; of this 5 oz. were given every 2 or 3 hours. Illness began 3 days previously with loose, mucous stools, averaging 10 a day, no blood, no vomiting. Temperature 100.5° F. Did not seem ill. Acid type of organism cultivated from stools. Patient was under observation 6 days. Child was given calomel and shortly after a dilute milk modification. After treatment was begun the stools were never more than 4 a day, were yellow and fecal but had mucus and a few curds. These disappeared and the child was discharged entirely well.

Moderately severe. R. W., 5 months old. Was nursed for 4 months, afterwards fed on 3 parts Straus' milk and 2 parts barley water, taking only 15 ounces of the mixture in 24 hours. The baby was in good general condition when taken sick 2 weeks before being brought to the clinic; the onset had been with vomiting and fever; there had been marked loss of flesh and the baby was markedly prostrated when first seen. The stools were from 5 to 7 a day, large, green with considerable mucus and some blood. Temperature 100° to 101° F. The "Flexner-Harris" type of organism was cultivated from the stools. The patient was under observation 9 days; was given calomel and the milk was stopped 2 days; then a weak milk modification was given. The stools became less frequent, their character improved and on the last day seen were only 2 in number, yellow and with some mucus. The temperature was normal.

Severe. M. K., 7 months old. Had been under observation for 6 months at the beginning of which time he weighed 4 pounds 15 ounces. Had been fed on various milk modifications and had gained very well; at the time of the attack was of fair weight and in good general condition. For about 10 days had suffered from symptoms of intestinal indigestion. The stools were yellow, frothy and large and there were 10 to 12 in 24 hours. There was some tenesmus and mucus in great amount, no blood. Free catharsis and the substitution of barley water for the milk had no effect; stools were still frequent and yellow and once contained a little blood. The true Shiga type of organism was found by culture from the stools. The temperature was always low never going above 100.4° F. Imperial Granum was no better borne than the barley. The child constantly failed and the stools were still frequent, as many as 16 in a day; bismuth only colored the stools. In a week the child was in desperate straits, eyes sunken, fontanel depressed and pulse imperceptible. He was given 20 c.c. of "Shiga" serum in the buttocks on 2 successive days. Stimulation by whiskey and strych-

nine and hot baths was resorted to. Child was also given a milk and water mixture 1 to 6. Very decided improvement was seen almost immediately, the number of stools diminishing in one day from 16 to 4; this was 3 days after the first injection of serum. From this time convalescence was rapid and 3 months after the attack he was a fat, well-nourished child, taking milk well and digesting it.

Fatal Cases.—To our knowledge there were 4 fatal cases. It is possible that some others of the cases observed died but not while under observation, nor were any in a moribund condition when last seen.

(1) J. C., 10 months old, in poor condition and emaciated; living in a tenement in fair surroundings but badly cared for; was taken with diarrhea while being fed a weak barley water and milk mixture. No history of previous illness, and he had been bottle fed for 8 months. The onset was without vomiting but with moderate fever and with frequent mucous stools, 8 a day, no blood. When first seen on the second day of the attack the baby was markedly anemic, fontanel depressed, heart very feeble; circulation poor; extremities cold; no distention. Lungs negative. Very restless. Milk stopped and barley water given and white of egg with whiskey. Temperature 101.8° F. Stools were small and green mucopurulent, with streaks of blood. Following day child was extremely prostrated; temperature 101° F.; edema of face and lower extremities; respiration shallow, radial pulse imperceptible. Death 36 hours later.

True Shiga type of the dysentery organism was separated from the stools on the first day of observation.

(2) G. H., 10 months old, in fair condition, living in a filthy tenement, with little sunlight and poor care; was taken sick while being fed a condensed milk mixture. He had been nursed until 3 months old. The onset was acute by vomiting, high fever, 103.5° F., and diarrhea; stools were 6 to 7 a day and contained mucus, no blood. When first seen, 4 days after the beginning of the attack, the child was somewhat emaciated; fontanel not sunken; temperature 103° F.; very restless and with some tenesmus. Put on barley water and following catharsis was given a bismuth mixture. On the seventh day of the attack was given 10 c.c. of "Harris" serum, and these injections were repeated on the eighth and ninth days. By the fourteenth day the general condition was somewhat improved, the temperature having fallen to 100° F., pulse still rapid. The diarrhea had much diminished so that there were only 2 or 3 yellow fecal stools a day. A weak milk mixture was given with no bad effect upon the intestinal condition, but the child gradually failed, and in spite of stimulation by whiskey and strychnia the extremities became cold, edema came on and the heart gradually gave out 4 weeks after the beginning of his attack. The mother was densely ignorant and failed to carry out directions, especially in regard to feeding; moreover she refused to have the child admitted to a hospital. The "Flexner-Harris" type of organism was separated from the stools on the first day of observation.

(3) A. K., 3 months old, fairly nourished, living in a clean tenement but with little care. Had been nursed entirely for one month. Was taken sick while being fed on Straus' sterilized milk. The onset was sudden with fever and diarrhea, no vomiting. Stools were mucous but contained no blood, 12 a day; there

was much tenesmus. First seen 7 days after the beginning of the attack; the child was anemic and in collapse. Fontanel depressed. Heart normal; lungs—fine râles at both bases behind. Child was admitted to the Babies' Hospital 4 days later and was given, along with other treatment, 10 c.c. of "Harris" serum. Refused food and later regurgitated after feeding. Temperature remained between 103° and 105° F. and the child died 48 hours later. The stools had diminished to 4 a day.

The "Flexner-Harris" type of organism was separated from the stools on the first day of observation.

(4) M. McK., 7 weeks old, a poorly nourished child, living in a dirty tenement with very poor care. Was taken sick with diarrhea while being fed on condensed milk and Eskay's food. The baby had been nursed for 3 weeks, but nursing had then been stopped because the mother developed an abscess of the breast. The onset was acute with vomiting but no fever. The stools were 5 to 7 in 24 hours, green, mucous and offensive, but contained no blood. When first seen, 7 days after the beginning of the attack, the child was much prostrated and anemic, temperature 100° F. and pulse 100 and weak, cold extremities and restless. After catharsis was fed on barley water, stools remained the same; refused food and in spite of stimulation and 10 c.c. of "Harris" serum the baby died 4 days later after having been in collapse for 24 hours.

Of the fatal cases all were under one year of age; were artificially fed and were in very poor condition when first observed, and also they had only the poorest care and attention.

Breast-fed Cases.—There were 14 infants exclusively breast-fed that suffered from infection with the *Bacillus dysenteriæ.*

(1) L. P., 6 weeks old, good general condition. Stools 4 to 8, watery, with slight amount of mucus, no blood. Five days after the beginning of the attack cathartics given and substitution of barley water for nursing; in 24 hours stools became fecal and the mucus disappeared. Never any vomiting or fever. The "Flexner-Harris" type of organism was isolated.

(2) F. A., 6 weeks old, good general condition. Diarrhea and vomiting. Stools soft and yellow with some mucus, 7 in 24 hours. Seen only once. The "Flexner-Harris" type of organism was isolated.

(3) P. B., 5 months old, good general condition. Onset without vomiting or fever. Three green, mucous stools daily. After calomel and withholding the breast the stools became yellow and fecal, 2 a day, and on the third day of treatment and the fifth of the disease the child was discharged perfectly well. The "Flexner-Harris" type of organism separated from the stools.

(4) C. F., 2½ months old, in good condition at the beginning of the attack. Onset with high fever, very frequent, green, fluid stools with curds and much mucus, no blood, 15 a day. Temperature 104° F. The "Flexner-Harris" type of organism found. Referred to hospital but did not go. Seen only once.

(5) D. M., 4 months old, in good general condition; 3 to 5 green and mucous stools, no blood; diarrhea began 2 days before coming under observation. No vomiting or fever; child not at all sick but the stools contained a little undigested milk and were green for 4 or 5 days. On the fourth and fifth days of treatment 10 c.c. of "Shiga" serum injected. Two days after this the stools be-

came yellow and fecal and the breast feeding, temporarily withheld, was resumed. The true Shiga bacilli were found in the stools.

(6) N. H., 8 weeks old, good general condition. Diarrhea with 6 to 8 fluid, mucous stools had begun 2 days before coming under observation. No fever or vomiting. Castor oil and barley water were followed by prompt recovery in 2 days. The "Flexner-Harris" type of organism was found.

(7) W. R., 8 weeks old, in good general condition. Diarrhea with fluid, mucous stools began without fever or vomiting 2 days before coming under observation. The exhibition of castor oil and barley water was followed by recovery on the fifth day of the attack. True Shiga organisms found in the stools.

(8) C. J., 3 months old, in good general condition. Diarrhea began without fever or vomiting, 3 days before coming under observation; stools 8 to 10 fluid and mucous, no blood. Castor oil and barley water effected a rapid cure in 2 days. The "Flexner-Harris" type of organism was isolated.

(9) L. G., 13 months old, fair general condition. Onset acute with fever 1 week before coming under observation, no vomiting. Stools had been 6 to 8 a day fluid and mucous, no blood, and child had lost much weight. Temperature 101.8° F. Calomel and barley water given. Case seen only once. The "Flexner-Harris" type of organism was isolated.

(10) J. D., 1 year old, good general condition. The attack of diarrhea began with vomiting and fever; stools 4 to 9 in 24 hours, loose, mucous, with slight amount of blood. When seen 1 week after beginning of attack temperature was 101° F. Child was somewhat prostrated and emaciated. Tenesmus and prolapse of rectum. Under treatment by castor oil and bismuth, the child improved rapidly.

(11) L. A., 10 weeks old, excellent general condition, had been sick for one week with diarrhea, 5 to 6 yellow, slightly mucous stools daily; no blood, no fever, no vomiting. Calomel and barley water effected a cure in 2 days, the stools being normal in 24 hours. The true Shiga and the "Flexner-Harris" type of organism were both present.

(12) R. A., 5 months old, good general condition. Diarrhea, 6 to 8 fluid mucous stools, without blood. No vomiting or fever. Came under observation on the third day of the attack. The giving of calomel, barley water and bismuth mixture for two days, followed by a gradual resumption of nursing effected a cure on the fifth day. The true Shiga type of organism was present.

(13) K. M., 8 months old, good general condition. Diarrhea without vomiting or fever. Stools fluid, mucous, no blood, 8 to 10 in 24 hours. Child sick 3 days before coming under observation; then calomel, bismuth mixture and barley water brought about a rapid recovery.

(14) C. S., 7 months old, excellent condition. Diarrhea with 8 or 9 fluid, very mucous stools without blood. On the eighth day of illness the child was brought to the clinic. Calomel and bismuth with barley water were followed by the reduction of stools to 3 in 24 hours and by the change in character to normal.

Of the breast-fed cases whose records are complete none died, all ran a very mild course, the average being 3 to 4 days after coming under observation. Save for the bacteriological findings these was nothing to indicate that their sickness, had any relation to true dysentery.

These cases, morever, with hardly an exception, were in well-nourished children. Blood was observed in but 1 case.

Type of Infection.—There were 42 cases in which the "Flexner-Harris" or acid-producing type of organism was found, 15 were infected with the alkaline or true Shiga type; in 5 cases both types of the organism were found. Of the 42 acid infections, 9 were classified as mild cases; 21 as moderately severe; 10 as severe, 2 not being classified. Of the 15 true Shiga infections, 5 were mild; 6 moderately severe and 4 severe. Of the 5 mixed infections 1 was mild and 4 moderately severe.

From this it will be seen that in the acid type of infection, as well as in the true Shiga type, the moderately severe cases were most numerous and there seemed to be no difference in the severity of the disease attributable to the type of infection.

We did not use at all, for diagnosis, the agglutination reaction of the blood of the patients. It has been proven in children as well as in adults that this reaction, while often present, is uncertain and unsatisfactory for the reason that it appears late, at the end of the first week, and often not before the second or third week and may disappear early in the prolonged cases; so that we can make our diagnosis by an examination of the stools much more easily and more satisfactorily than by the blood of the patient.

Treatment.—As outlined above the majority of the cases were treated by the usual methods both as to their management and diet. Milk, whether breast milk or cow's milk was immediately discontinued; barley water, broth or some proprietary food or, rarely, albumen water being given in its place; it was only resumed when the acute symptoms had subsided. Catharsis by calomel and castor oil was the invariable rule. When there was great irritability of the intestines with tenesmus and numerous small stools, rectal irrigations without or with paregoric were employed. For temperature that gave rise to nervous symptoms irrigations and alcohol sponging were resorted to. A bismuth mixture was used in a few cases.

Serum Therapy.—There were in all 10 cases in which the serum was injected; 4 were infections with the acid type of organism and were given "Harris" serum; 6 were infections with true Shiga organism and were given "Shiga" serum. Only the severe cases were subjected to this treatment as it was found that in dispensary practice the mothers would not return with the patients after injection unless the disease was apparently serious.

Of the injected series, cases (1) and (2) were given 10 c.c. of

"Harris" serum and did not return after the injections. Case (3) after receiving 20 c.c. of "Harris" serum showed decided improvement; after the injection of 10 c.c. additional this was still more marked but the child died of marasmus three weeks later without any return of the diarrhea. Case (4) was already improving on irrigations before the injection of the serum so that no conclusions can be drawn. Case (5) showed decided reduction in the number of stools and improvement in their character after the injection of 10 c.c. of "Shiga" serum on 2 successive days. Case (6) received 20 c.c. of "Shiga" serum; but the improvement in the child's condition could not be attributed to the injection.

Case (7) received 10 c.c. of "Harris" serum when moribund.

Case (8) (the severe case quoted above) improved very markedly after 2 injections of 20 c.c each of "Shiga" serum, but only after an interval of 3 days, during which time there was additional stimulation and change of diet, so that the effect of the serum is doubtful.

Cases (9) and (10) were apparently uninfluenced by the injection of "Shiga" serum.

A rash similar to that seen after the employment of diphtheria antitoxin was observed in only one patient, notwithstanding the fact that the quantity of serum injected was very much greater than that ordinarily used in diphtheria.

The difficulties of administering the serum in outdoor practice must be emphasized. The quantity of serum of the present strength necessarily employed is large and must often be injected into an emaciated child, producing a swelling of a size alarming to the laity. Objection also arises on account of the pain of the injection.

From an analysis of these 62 cases observed by us, it seems that certain points are worthy of special note.

(1) The unexpectedly great prevalence of the dysentery organism in cases of diarrhea in infants, at least during the summer months. Thus out of 64 consecutive cases examined in the Vanderbilt Clinic 62 were positive.

As has been mentioned before this is the first large series of cases examined seriatim that has been made and the result is certainly striking. It is all the more so when we consider that these were cases in dispensary practice where, with the severe, the very mildest cases may be seen. Duval and Bassett examined 25 successive cases and found the organism in 19, but it should be stated that the patients were observed in a sanitorium at a distance from Baltimore where, of course, only the more severe cases were sent from the dispensaries, while ours were

all ambulant patients and their stools were examined whenever there was the slightest sign of any digestive disturbance. Our cases were also seen very early whereas, in hospitals, the cases are rarely seen until after their initial symptoms have passed.

(2) All types of diarrheal disease, as characterized by their clinical symptoms, are to be found among these cases. Some were examples of severe and some of mild ileo-colitis; others could only be classed as the mildest form of intestinal indigestion. The course of the disease, while usually short, was prolonged in 8 cases.

(3) As compared with cases of summer diarrhea of other years those in this series were in general much milder and possibly this was due to two factors: (*a*) The cool summer. (*b*) The increasing knowledge among the tenement population of the care of infants and their food.

(4) The striking number of breast-fed infants, 14 in 62 cases, more than 20 per cent. of all.

In the series of Duval and Bassett previously mentioned there were 4 breast-fed cases and a few others in addition have been reported. The great number in our series is accounted for by the fact that all stools from patients with diarrhea were examined. As will be remembered of our 14 breast-fed children not one was severely or even moderately ill, and only one had blood in the stools. Such cases would therefore not be sent to hospitals and so usually their stools would not be available for examination.

(5) The serum treatment was not given in a sufficient number of cases to warrant any conclusions. While of apparent benefit in some cases there were others in which no effect whatever was noticed. It may be that larger dosage is necessary; but, if so, the serum must be more concentrated than at present.

A CLINICAL STUDY OF THE CASES OF DIARRHEA PRODUCED BY BACILLUS DYSENTERIÆ (SHIGA), TREATED DURING THE SUMMER OF 1903 AT THE THOMAS WILSON SANITARIUM.*

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During the summer of 1902 Duval and Bassett, working in the laboratory of the Thomas Wilson Sanitarium under a grant from the Rockefeller Institute for Medical Research, were able to isolate the Bacillus dysenteriæ (Shiga) from the dejecta of forty-two infants suffering from diarrheal disorders. Last summer the work was continued by Bassett, who succeeded in finding the same organism in the stools of upwards of forty similar cases. His report appears as a separate paper, as does that of Winne, late assistant resident physician at the Sanitarium, which gives the results of observations made on the agglutination reaction of the dysentery bacilli isolated, tested with the blood of these patients as well as with anti-dysenteric serum.

The cases were not examined seriatim, but nearly every case that had a history of acute diarrhea, as well as those whose stools contained mucus, pus, and blood, was tested bacteriologically.

As will be seen later the majority of our cases were severe or had persisted a long time before coming under observation. This is accounted for by the fact that the Sanitarium is at some distance from the city and the mild cases and those responding readily to treatment are cared for in the dispensaries of the city.

This report will be confined to a consideration of the clinical features presented by the cases, forty-three in number, in which the specific organism was demonstrated in the stools.

Previous Attacks of Diarrhea.—There was but a single instance among our cases in which there had been a history of diarrhea previous to the one from which the patient was suffering on admission;

*The Thomas Wilson Sanitarium is situated in the country ten miles from Baltimore, where each summer are treated from 300 to 400 infants and young children suffering from gastro-intestinal disorders.

i.e., the children were brought to the Sanitarium during their first illness. Moreover, there was no history of any one in the household other than the baby suffering from diarrheal disorders. The illness of the infant was the first, and usually the only case of intestinal disease in the family—a point of some importance in considering the mode of infection.

Character of the Food and Hygienic Surroundings at Time of Attack.—An especial effort was made to ascertain the nature of the previous surroundings of the patient and the character of his diet. In many instances reports were obtained from nurses employed by the Sanitarium who visited the patients in their homes. These factors have been gathered together in the accompanying table. It should be stated that our patients come largely from the middle class of working people of Baltimore.

FOOD AND HYGIENE.

Food at Time of Illness.	Total.	Hygienic Condition.			Refrigeration.		Water with or Between Feedings.		
		Good.	Fair.	Bad.	Ice.	No Ice.	Boiled.	Unboiled.	Never Given
Breast, exclusively	2	0	0	2	0	0	0	1	1
Cow's milk (fair) heated	11	5	5	1	7	2	2	7	2
Cow's milk (fair) raw	6	1	3	2	1	3	0	5	1
Cow's milk (store) heated	4	0	2	2	1	3	2	2	0
Cow's milk (store) raw	5	0	3	2	0	5	0	4	1
Condensed milk	14	5	5	4	1	6	4	10	0
Table diet	1	1	0	0	0	0	0	1	0
	43	12	18	13	10	19	8	30	5

The milk marked "store" in the preceding table was bought for the babies at small grocery stores. It was grossly contaminated, having a bacterial content of more than 5,000,000 per c.c. The milk marked "fair" was delivered at the homes from a wagon or bought at a dairy store. It contained often 500,000 to 1,000,000 bacteria to the c.c. at time of delivery. The "heating" mentioned usually meant that the milk was scalded or brought to a boil over the fire. In no case was steam sterilization or Pasteurization employed.

Although too much stress should not be laid upon the tabulation of a short series of cases it is surprising to learn that the quality of the milk or the nature of the child's surroundings seemed to make little

difference in the number of cases admitted. Moreover, the milk given many of these children, though fair, was never of the first quality. But after due weight is attached to these facts, the discrepancy between the number of cases, on the one hand, and the character of the food and the hygienic surroundings, on the other, makes it difficult to charge either to the food or to the daily care of the infant alone, this outbreak of diarrheal diseases due to the dysentery bacillus.

A primary infection of the whole milk supply of the community is an impossible hypothesis, as our patients lived in widely separated sections of the city and obtained their milk from a large number of remote sources. Moreover, most of it was heated before using, and many, fed exclusively on condensed milk, received no fresh milk at all.

Condition of the Patient Previous to Illness.—Very rarely, in but two instances, was there definite discoverable cause for the attack. The diarrheal disorder was usually the infant's first acute illness. However, fully 25 out of the 43 cases were poorly nourished and showed pronounced stigmata of rickets, while 10 were markedly emaciated. The frequent history was that the baby for some weeks or months had not been thriving and had lost in weight, when, without any immediate cause to which the mother could attribute it, symptoms indicative of gastro-intestinal disease set in.

Length of Symptoms Before Observation.—The series of cases can be divided into the following groups with reference to the duration of the disease before observation:

1-10 days	10-20 days	More than 20 days
13	11	19

But one case was seen the first day of illness and only four before the sixth day.

Length of Time Under Observation.—The time these cases were under observation varied from 1 to 47 days, the average stay at the Sanitarium for the whole series being 17 days. The more protracted cases occurred, as a rule, late in the summer.

The Symptoms of the Attack, characterizing the cases as very mild, moderate, and severe. Our experience would indicate that the dysentery bacillus in the infant's intestinal tract may produce widely different clinical manifestations, apparently identical with the various forms of the familiar so-called "summer diarrhea." Our cases have been roughly divided into two groups, those in which the toxic phenomena are most marked and those in which there is evidence of serious lesions

of the intestinal wall. Each of these divisions may be mild, moderate or severe.

	Mild.	Moderate.	Severe.
Toxic cases	5	6	10
Ileo-colitis	0	8	14
	5	14	24

Other frequent symptoms are:

	Absent.	Moderate.	Severe.
Vomiting	9	22	12
Diarrhea	0 (1)	25 (2)	18 (3)
Fever	0 (4)	17 (5)	26 (6)

(1) Less than 4 stools in 24 hrs. (4) Temperature not over 99°
(2) 4-15 " " " " (5) " between 99° and 101°
(3) More than 15 " " " " (6) " higher than 101°

The character of the stools is thus briefly indicated:

	None.	Trace.	Moderate.	Much.
Mucus	0	4	30	9
Blood	15	10	16	2
Pus	10	10	15	8

Complications were comparatively rare. Convulsions occurred as the terminal event in three cases. Broncho-pneumonia was recognized but twice; one child died of intestinal obstruction, and one developed pyemia. In six instances a patient was readmitted because of a relapse of the disease after apparent cure.

Type of Organism.—In all our cases, as is brought out in Bassett's report, only the so-called "Flexner-Harris" or acid-producing type of the organism was isolated; that is, the one which ferments mannite with acid production.

The Results in our series, arranged according to the form of the infection, are as follows:

		Well.	Improved.	Unimproved.	Died.
Toxic Type....	Mild.....	3	2	0	0
	Moderate.....	3	3	0	0
	Severe.....	2	5	0	3
Inflammatory Type.....	Mild.....	0	0	0	0
	Moderate.....	3	1	0	4
	Severe	2	1	1	10
		13	12	1	17

Thus, it is seen that of a total mortality of 17, or 39 per cent., the large majority, 14, occurred in the cases of ileo-colitis, most of which were admitted late in the summer.

It is well known that many of these cases begin with simple gastro-enteritis; and the difference in the results obtained in the treatment of the two forms of intestinal disease argues strongly the importance of prompt abortive measures.

The relation of the previous diet to the results is thus indicated:

		Well.	Improved.	Unimproved.	Died.
Cow's milk of all kinds raw and heated.....	26	10	7	1	8
Condensed milk.....	14	1	5	0	8
Table diet.....	1	1	0	0	0
Breast exclusively.....	2	1	0	0	1
	43	13	12	1	17

It is to be noted that of the 14 cases previously fed on condensed milk, 8, or 57 per cent., died at the Sanitarium in spite of treatment, and but one really recovered; while of the 26 cases fed on cow's milk at their homes, 8, or 29 per cent., died and 10 were permanently cured. That is, that although the condensed milk infants are perhaps less liable to infection with the dysentery bacillus, when the organisms find entrance the children so fed have less resistance.

Age in Months.	Duration of Illness Before Injection, in days.	Number of Injections.	Total Amount of Serum in c.c.	Duration of Serum Treatment in Days.	Variety of Serum.	General Condition of Patient at First Injection.	Result of Serum Treatment.	Condition on Discharge.
6	1	7	120	20	S.	Acute attack at sanitarium in marantic infant	Favorable. Fewer stools. Brighter	Unimproved.
14	9	7	110	14	S.	Comatose ; irregular pulse, mucus and blood in stools.	Slightly favorable. Slow recovery	Well.
4	4	5	50	7	H.	Poorly nourished, collapsed. Extremities cold	Favorable	Well.
2½	6	1	10	1	H.	Poorly nourished, listless	Favorable, brighter. Recovery prompt	Well.
5	10	5	60	8	H.	Poorly nourished, collapsed	Favorable. Lower temperature	Well.
17	25	3	30	4	H.	Fair condition. Numerous stools containing mucus and blood	No immediate improvement	Improved.
6	10	2	40	2	S.	Fair condition	Serum of doubtful effect	Improved.
7	14	6	110	7	H.	Collapsed, semi-comatose	Action of serum, if any, slow. Temperature reduced	Improved.
8	50	4	40	3	H.	Poorly nourished. Muco-purulent stools, with blood	Slow. Doubtful	Improved.
3	16	2	20	2	H.	Poorly nourished, feeble	Inert or slightly helpful	Improved.
5	7	3	30	3	S.	Emaciated, drowsy	Serum seemed at first helpful, later inert	Died.
2½	22	6	100	21	S. and H.	Poorly nourished. Extremities cold	Serum inert	Died.
6	30	8	170	18	S.	Collapsed, semi-comatose	At first helpful, then inert	Died.
7	14	14	230	16	S. and H.	Poorly nourished. Furunculosis	Inert	Unimproved.
3½	15	3	60	3	S. and H.	Emaciated, collapsed	Inert	Died.
4	30	13	200	20	H.	Collapsed, drowsy	Inert	Died.
6	30	5	70	10	H.	Emaciated. Marked rickets. Drowsy	Improvement (?) first, inert later	Died.
12	22	7	90	11	S. and H.	Poorly nourished	Inert	Died.
9	17	3	40	3	S.	Poorly nourished	Inert. (Broncho-pneumonia.)	Died.
12	30	4	60	4	S.	Collapsed, sunken fontanel. Many stools	Inert	Died.

Cases Exclusively Breast-fed.—Two cases only occurred in this series:

1. Girl, ten weeks old, a twin (other died at birth). Family very poor and care wretched. Child had never been well nourished. Illness began three weeks before admittance. Stools were green, six to seven a day, with mucus, no blood. Considerable vomiting and colic.

After an observation of two weeks, in which the child was carefully fed and treated according to the ordinary methods without serum, she was discharged, improved.

2. Boy, six months old. Child had never been well nourished, always sickly. Mother weak and anemic, living in poor surroundings. Child nursed very irregularly. Illness began three weeks before admission, with diarrhea, no vomiting. Stools, four to six a day, containing mucus, no blood.

On admission the child was markedly emaciated, with pronounced signs of rachitis. Temperature varied from 96°-101° F.

Serum was given without effect, and at the end of two weeks the child died. This was apparently a terminal infection in the course of marasmus.

Serum Treatment.—Through the kindness of Dr. Flexner and the generosity of the Rockefeller Institute for Medical Research, the Sanitarium was supplied with antidysenteric serum obtained from horses immunized against both types of the organism.

Because of the distance of the Sanitarium from Baltimore, but few early cases come under observation, so little selection could be made of infants favorable for this treatment.

Eliminating a number of instances in which the serum was given when the patient was in extremis or when serious complications obscured its action, twenty cases remain to be recorded. The preceding table contains the more important data with reference to the use of the serum.

The variety of the serum is designated by the letter S or H, indicating serum made from organisms of the "Shiga" or "Harris" type, respectively.

Cases Treated by Serum Injection.—(Vide table on page 153.)

The results obtained with the antidysenteric serum were in our hands disappointing. It seemed, however, to have a slightly favorable action in those of the cases in which it was employed early in the disease, particularly in the first case, in which the infection took place at the Sanitarium, when, in a markedly emaciated infant, there was definite improvement noticed in six hours following the injection of the serum; in the great majority of the cases, however, it seemed to be without effect.

A CLINICAL REPORT OF TWENTY-SIX CASES OF INTESTINAL INFECTION WITH THE BACILLUS DYSENTERIAE.

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Two of the twenty-six cases here described were seen in the wards of the Nursery and Child's Hospital, one in the Babies' Hospital Dispensary, seven in the wards of the New York Infirmary for Women and Children and sixteen in the Out Door Department of the same Institution.

The acid-producing or "Flexner-Harris" type of the Bacillus dysenteriae was found in twenty-five cases, the true Shiga type in one.

The symptoms of the infection in this one case differed in no way from those observed in the twenty-five others.

Mild as well as severe cases of intestinal disturbances were studied.

One case occurred in June, thirteen in July, ten in August and two in September.

Age of Patients.—Under 6 months, 4; from 6 to 12 months, 5; from 12 to 18 months, 5; from 18 months to 2½ years, 10. Two cases were in children aged five and ten years respectively.

Previous Diarrhea.—A history of previous attacks of diarrhea was obtained in 6 cases; in 17 no previous attack had occurred, and in 3 no trustworthy history of previous diarrhea could be obtained.

Condition at the Beginning of the Attack.—Was good in 11; fair in 4; poor in 9; not recorded in 2.

Character of the Food.—None of the children were exclusively breast-fed at the time of the attack. Of the four children under six months old, three had never been nursed and one was breast fed for three weeks only.

Of the 5 infants between six and twelve months old, one received grocer's milk, one condensed milk (a change to Straus' milk having been made shortly before the illness began); one was fed upon grocer's milk and eggs; and one upon bottled milk, macaroni, eggs, bread and soup. In this series one infant had been nursed to within a few days of the illness and the change of nourishment was probably a

predisposing factor in determining the attack. The 5 infants from twelve to eighteen months old received "a little of everything"; 4 had been breast-fed to ages varying from twelve to sixteen months; 2 were weaned one month previous to the beginning of illness; 1 was receiving the breast in addition to light general diet at the time of the attack.

The 10 children ranging from eighteen months to two and one-half years had all been breast-fed for from nine to twenty months.

When taken ill 2 of these children were receiving house diet, 2 milk with bread or cereals, 4 light general diet, and 1 condensed milk; in one case the food was not recorded.

In the 2 cases five and ten years old no special cause for the attack was discoverable.

As to environment, under which term are included cleanliness, ventilation, sunlight and care, this was: good in 2 cases; fair in 8; poor in 7; bad in 3; not noted in 6.

The duration of the symptoms before the cases came under observation was: less than 1 week in 9; 1 week in 4; 10 days to 2 weeks in 4; 3 weeks in 3; 1 month to five weeks in 3; not noted, 3.

The patients were under observation: less than 1 week, 4; 1 week, 3; 2 to 3 weeks, 8; 4 to 6 weeks, 3; not noted, 8.

The cases are grouped under three heads: mild, moderately severe and severe; of the latter there were five cases all of which terminated fatally. This classification is based not so much upon the frequency as upon the character of the stools and more especially upon the general constitutional symptoms.

The mild cases, 8 in number, were those the number of whose stools was as a rule four to seven, consisting of green and yellow feces with, at times, a slight or moderate amount of mucus. The temperature, in these cases, did not rise about 100°, tenesmus was absent and slight tympanites rarely present. There were no nervous symptoms and recovery occurred in from one week to two months.

In the 13 cases classed as moderately severe, the stools usually numbered from five to fifteen, consisted of green and yellow feces with a considerable amount of mucus and in two cases a slight admixture of blood.

The temperature as a rule remained below 102°; tenesmus and nervous symptoms were observed at times.

In the 5 severe cases the stools varied from seven to twelve, at times containing blood and showing in three cases a tendency to become watery. The temperature ranged from subnormal to 106°; tenesmus

and tympanites were generally marked and nervous symptoms prominent.

The treatment was chiefly dietetic. Calomel and castor oil were frequently employed and bismuth subnitrate was given in some cases.

Rectal irrigation of saline solution was employed for great toxemia or tenesmus.

In one severe case the serum treatment was tried.

A brief record of four severe and fatal cases is appended; the fifth fatal case was seen in the Infirmary Dispensary and died one day later.

M. S., three months old; condition poor at the beginning of the attack. Brought to the New York Infirmary from a dirty, practically sunless, poorly ventilated tenement; care had been fair and there had been no previous diarrhea. The infant had been nursed three weeks, receiving after that time condensed milk and occasionally zwieback.

The onset was by vomiting. On admission: anemic; fontanel depressed. Stools seven to eight: green and yellow feces, much mucus, no blood. Discharged at the end of two weeks cured.

Readmitted July 30th, emaciated and much prostrated (attack of chicken pox had occurred in interim), extremities cold; stools six to ten, brown and watery, no mucus and no blood; temperature range from subnormal to 103°. One day after admission 10 c.c. of the "Harris" anti-dysenteric serum were injected and this was repeated on two succeeding days. A diminution in the number of stools took place and there was an amelioration of the general symptoms which in all probability was largely due to energetic stimulation. On the third day after admission the physical signs of broncho-pneumonia were noted and death followed three days later.

An autopsy revealed acute broncho-pneumonia and follicular entero-colitis.

L. P., nine months old; never nursed; he received besides the bottle, macaroni, eggs, bread and soup. Condition at the beginning of the attack fair, but infant rachitic. No previous diarrhea; duration of the attack eleven days.

On admission, August 5th, physical signs of broncho-pneumonia.

Fontanel somewhat depressed. Ten to twelve stools in twenty-four hours: green, feces, very little mucus, some blood; tympanites present; temperature 101-106°; nervous symptoms noted. Under observation six days. Death August 11th. Autopsy showed acute broncho-pneumonia and follicular colitis.

The Peyer's patches in the ileum were slightly enlarged; solitary follicles in the colon enlarged, many beginning to break down in the center. Mesenteric lymph nodes moderately enlarged.

S. D., four months; never breast-fed, Straus' milk given every two hours. Home surroundings and care fair. No previous diarrhea. Duration of illness one week; onset by vomiting. Admitted to Infirmary on September 7th. Anemic; rachitic; fontanel slightly depressed; tongue coated; lungs and heart negative. Four to ten stools consisting of semi-solid green and yellow feces, much mucus and no blood; tympanites was marked. The temperature varied from 98-104° F. Death occurred on September 28th. An autopsy could not be obtained.

S. C., four months; never nursed; fed on grocer's milk. Condition at the beginning of the attack, poor. Surroundings very unfavorable and care poor. No previous diarrhea. Admitted to the Infirmary on September 3d. Duration of illness one week. Condition on admission: anemic, fontanel depressed, circulation poor. Lungs and heart negative; five to ten stools a day consisting of green and yellow feces with much mucus, no blood; no tenesmus, no tympanites. Discharged September 27th, much improved and steadily gaining in weight. Brought back to hospital on October 20th, moribund; death occurred on the same day. The second attack began with vomiting three days before admission. The stools were green and watery and numbered six in twenty-four hours.

Autopsy showed congestion and edema of the lungs and ulcerative colitis.

In conclusion, I desire to call attention to the frequent occurrence of the *Bacillus dysenteriæ* in the mildest types of intestinal disorder.

It is interesting to note that of the five fatal cases, all of which were under nine months old, not one had been breast-fed. One infant was nursed for three weeks only.

As the serum treatment was employed in but one case, no opinion can be formed as to its efficacy.

I desire to thank Dr. Annie S. Daniel and Dr. Ethel Brown for placing material from out-practice cases as well as the histories of the same at my disposal. Dr. Marie Grund rendered valuable assistance in obtaining complete histories. To Dr. R. G. Freeman's courtesy are due the records obtained from the Nursery and Child's Hospital.

CLINICAL REPORT OF NINETEEN CASES OF INTESTINAL INFECTION, WITH THE BACILLUS DYSENTERIÆ.

BY SAMUEL AMBERG, M.D., OF BALTIMORE,
Associate in Pediatrics, Johns Hopkins University.

The total number of cases in which the bacteriological examination of the stools was made was 47. In 19 of these cases the Bacillus dysenteriæ (Shiga) was found. This report will only consider positive cases.

One case occurred in a boy nine years of age. All of the other cases were under two years of age.

Previous attacks of diarrhea were noted in 3 cases. It may be well to call attention to the fact that satisfactory histories, in regard to this point, could not always be obtained.

Food at the Time of Attack.—In only one instance did the food consist of breast milk alone. Several other infants had breast milk, but also in addition other food, often improper. The hygienic surroundings and the care given to the patients were, in many instances, poor. The food was evidently improper in 6 cases; in 5 the food had been regulated by the family physician. One patient who had suffered from diarrhea during the previous summer was on a very strict regimen.

In regard to the quality of the cow's milk given, it may be stated that those seen in private practice received bottled milk from the best dairies in town. Of the other cases one received grocery milk, while the supply of the remainder was not ascertained.

Exciting Cause of the Attack.—The chief factors entering into consideration are the feeding and the hygienic conditions. In 6 cases taken from private practice there is no apparent reason to assume such a cause. In the dispensary cases, which represent the poorer classes, both the feeding and the conditions of life were such that it was not surprising to see these infants the subjects of gastro-intestinal disturbance.

Type of Disease.—The classification of 5 cases of the total 18 (the case of the boy of nine years being omitted) as mild, rests on the facts

that the condition of the infants at the time of observation was good or fairly good; that the number of passages had not exceeded twelve in twenty-four hours, and that with the exception of 1 case tenesmus was absent. Furthermore, blood was not present in the passages.

The course of the disease could not be followed in 2 cases; 2 others recovered in three to four weeks. In only one case was vomiting a marked symptom. In this the recovery was not complete after fifty-one days' observation, though the symptoms were never severe. The number of leucocytes in the dejecta varied much, but sometimes they were very numerous.

The condition of the 7 cases classified as moderately severe was good in 5, fairly good in 1, and poor in 1 case. The number of passages varied from ten to twenty in twenty-four hours; tenesmus was present in 3 cases, absent in 4. None of the babies vomited very much. The passages usually contained small amounts of fecal matter and curds. The amount of mucus was considerable. The number of leucocytes was great, and with the exception of two cases more or less pus was discernible to the eye, but rarely after the third day of observation, and then only in small quantity.

Blood was noted in the passages of all cases but one. This case was placed in this group mainly on account of the course of the disease, during which the weight dropped from 12 lbs. 1 ounce to 8 lbs. 9 ounces.

There were 6 classified as severe. The condition of these was good in 2, fairly good in 2 and poor in 2. The stools of these patients were usually frequent, four to sixteen in twenty-four hours. Here, too, vomiting was not a prominent feature. Tenesmus was present in all cases but one, and one child seemed to have constant pain in the abdomen. In general the character of the passages did not differ materially from those of the moderate group. One case did not have blood in the stools, but the severe course of the disease places it in this group. One was classified as a severe case on account of the amount of pus present in the stools and the protracted course of the disease accompanied by considerable emaciation. The amount of blood in the stools of these patients was never large and never were there any clots. Pus was constantly present in one case, though in varying amount, and the number of the passages did not decrease materially during the course of the disease.

Type of Organism.—The type of dysentery bacillus found in 17 of the 18 cases was the "Flexner-Harris" or acid-producing type and in 1 the true Shiga type was isolated.

Of the 18 positive cases, 4 died. The disease in one took a rapid course and was associated with a high temperature. The autopsy of one case revealed the typical lesions of a follicular ileo-colitis.

Serum Treatment.—There were in all 10 cases treated by the injection of serum. This does not include the boy nine years old, who died despite several injections of "Shiga" serum.

All patients with one exception were injected on the first day of observation. The exception was Case IX, injected on the third day.

A short description of each case follows:

I.—Poorly nourished infant, seven months old. Moderately ill two weeks before coming under observation. Given "Harris" serum, 10 c.c., on four occasions. In twelve days discharged apparently cured. "Flexner-Harris" organism isolated.

II.—Poorly nourished infant, five months old. Sick one week before coming to dispensary. Under treatment one month, during which time "Shiga" serum was given four times, 50 c.c. in all. Infection was with the "Flexner-Harris" type of organism. Fatal termination.

III.—Well nourished child, twelve months old; observed on the first day of attack. Severely infected with the true Shiga type of organism. "Harris" serum given, 10 c.c., two different times. Child made a good recovery in ten days.

IV.—Well nourished child, nineteen months old; seen on second day of attack; given "Harris" serum, 10 c.c., three times. Was moderately ill and under observation one month, at the end of which time he was discharged cured. "Flexner-Harris" organism obtained from stools.

V.—Fairly nourished child, six months old, who had been moderately ill for one month before treatment; had two injections of serum. He received 10 c.c. of "Harris" serum on one occasion and 10 c.c. of "Seward" serum on another. The infection was of the "Flexner-Harris" type. He was under treatment six weeks and was discharged improved but not entirely well.

VI.—Well nourished child of nineteen months. Seen on the fourth day of a moderately severe attack. "Flexner-Harris" type of organism isolated. Treated by injection of "Seward" serum, 15 c.c., on two occasions. Discharged cured in eight days.

VII.—Fairly nourished child, eighteen months old. Had been severely sick four days with a "Flexner-Harris" infection. Received 10 c.c. of "Shiga" serum on the first and second days of observation. No benefit seen from this. Was discharged at the end of a month and a half, improved.

VIII.—Twenty months old. Well nourished; sick six days before coming under observation and under observation twenty days. Ten c.c. of "Seward" serum given on the first and second days of observation. Discharged cured in twenty days. "Flexner-Harris" type of infection.

IX.—Twenty months old; well nourished. Sick one week before coming under observation. Was given "Shiga" serum, 20 c.c., and "Seward" serum, 25 c.c., in five successive injections. No improvement and the child died at the end of seventeen days. "Flexner-Harris" type of infection.

X.—Ten months old; well nourished; sick ten days before coming under observation, but only moderately so. Was given two injections of 25 c.c. of

"Seward" serum. Child discharged cured in five days. "Flexner-Harris" type of organism isolated.

The small number of cases under observation and the fact that the usual treatment was given beside the serum makes it impossible to draw definite conclusions in regard to the effect of serum treatment. Case III. improved very rapidly after the administration of serum, but in none of the others was any striking benefit noticed. No ill effects were seen in any case.

REPORT OF SEVEN CASES OF INTESTINAL INFECTION WITH THE BACILLUS DYSENTERIAE (SHIGA) OCCURRING AT THE NEW YORK FOUNDLING HOSPITAL, WHICH WERE TREATED WITH ANTIDYSENTERIC SERUM.

BY ROWLAND G. FREEMAN, M.D.,
Attending Physician to the New York Foundling Hospital.

Case I.—Seven months old, admitted June 15, 1903. A poorly nourished, rachitic child, weighing only 9 lbs. He had diarrhea; the stools were green, with mucus and curds, occasionally fluid, three to five in twenty-four hours. There was no vomiting, temperature between 97.5° F. and 100.5° F. This condition persisted for one month.

On July 17th his temperature began to rise, fluctuating between 100° F. and 105° F. The stools did not increase in number, but on July 21st began to contain blood, which soon became very abundant. The *B. dysenteriæ* was isolated from the stools. He was given "Harris" serum, 10 c.c., on six successive days. Blood continued for seven days and then disappeared. The stools were from two to five a day, and after two weeks improved very much in character, so that they were yellow, brown and formed, though still containing some mucus. Thereafter there was no rise in temperature. His weight varied but slightly for the next three months, a few ounces being gained and then lost. He eventually died of marasmus on November 6th. No autopsy was obtained. In this case there seemed to be some benefit from the use of the serum, but the child was unable to overcome his marantic condition.

Case II.—A well-nourished child, seven months old, suddenly became ill with temperature of 103° F., rising in twenty-four hours to 104.8° F. The stools at first were brown and loose, two to four a day. The temperature then dropped to normal, and after three days the stools were normal for twenty-four hours; but a day later a relapse occurred, the stools became frequent and green, with mucus and blood, and the temperature rose to 103° F. The child thereafter lost ground rapidly and died, despite the injection of 10 c.c. of "Harris" and 10 c.c. of "Seward" serum. The temperature for the last three days was considerably elevated.

The *B. dysenteriæ* was found in the stools five days before death, and was also cultivated from the post-mortem scrapings of the intestinal mucosa. The autopsy showed an acute ileo-colitis with superficial necrosis and hemorrhages.

Case III.—One year old. Following measles and after her temperature had become normal there occurred numerous green mucous stools, without blood; from these the *B. dysenteriæ* was isolated. The temperature at first was very

high, varying between 100° F. and 104.6° F.; after seven days it fell to normal. Blood was present in the stools, but never in considerable quantity. There were never more than five stools in twenty-four hours. She was given on successive days "Seward," "Harris," and "Shiga" serum, 100 c.c. in all. There was no improvement seen from the injections and her temperature during the last ten days was very irregular, occasionally reaching 104° F. The disease was complicated by the development of diphtheria one week before death. As this was laryngeal, pneumonia had developed before it was discovered and diphtheria antitoxin was used too late to be effective. Death occurred twenty days after the beginning of diarrhea.

The autopsy showed membranous ileo-colitis.

Case IV.—A very small, poorly nourished child, fifteen months old, weighing 12 lbs., was suddenly taken ill with green, mucous stools. There was no vomiting; temperature below 100° F. until the twelfth day, when blood appeared in the stools, and coincident with this, a rise in temperature to 103° F. Culture showed *B. dysenteriæ*. He was given Shiga serum, 10 c.c., on five successive days, but the temperature did not fall, remaining about 101° F. and the frequent mucous green stools with blood continued. He died one week later. No autopsy.

Case V.—A very poorly nourished child, seventeen months old, weighing 13½ lbs., was brought to the hospital with the following history: He had been sick for several weeks with loose brown stools containing mucus but no blood. He had been losing weight and had been feverish for some time. His temperature after admission was irregular, but for the first four weeks that he was under observation, never high. An examination of the stools failed to show the presence of the *B. dysenteriæ*. At the end of three weeks his temperature began to rise, the stools to become more frequent and to contain an increased quantity of mucus and a small amount of blood. He was given on successive days "Harris" or "Shiga" serum until he had had in all 75 c.c. of "Harris" and 30 c.c of "Shiga" serum; the blood disappeared from the stools and the temperature fell almost to normal, but he died with general edema and marked emaciation. *B. dysenteriæ* was found in the stools five days before death. No autopsy.

Case VI.—A fairly nourished child nine months old was brought to the hospital, having had an attack of measles one week before. She had a high temperature (104° F.) and frequent green watery stools, containing at times mucus and a slight amount of blood. There was only a little vomiting. Examination of the stools for *B. dysenteriæ* gave a positive result. "Seward" serum was given, 5 or 10 c.c., on successive days, without affecting in the slightest way the course of the disease. Her temperature remained constantly high, between 101° F. and 103° F. The frequent stools continued, prostration became very marked and she developed signs of broncho-pneumonia and died after fifteen days of observation. In all 106 c.c of serum were given. No autopsy.

Case VII.—A nursing child, one year old, was taken suddenly ill with frequent greenish-yellow stools, four to six a day. They contained blood and mucus. There was no vomiting. Temperature not high, averaging 98°-100½° F. *B. dysenteriæ* was found in the stools. She was given "Shiga" serum, 35 c.c. in all, in 5 c.c. doses. At the end of sixteen days there was a sudden rise of tem-

perature to 104° F., and it remained high for four days, but after this fell to normal. The stools gradually became normal in appearance and the case went on to complete recovery.

From an examination of the reports it does not appear that there was demonstrated in any a marked curative effect from the serum. Case I. was undoubtedly improved by it and Case V. to a less degree; but both of these eventually died of marasmus some time after the subsidence of their intestinal symptoms. Case III. was complicated by diphtheria and broncho-pneumonia and death was due directly to these complications. Cases II., IV., and VI. died as a direct result of the intestinal disease; one of these children, however, was in wretched condition before the attack and incapable of withstanding any serious illness. Almost all of the children were poorly nourished infants of the type known as "institution children" and their failure to respond satisfactorily to any remedial measures is not surprising. The only recovery was in a well-nourished, breast-fed infant, with a mild type of infection.

SEVEN CASES OF INTESTINAL INFECTION WITH THE BACILLUS DYSENTERIAE TREATED BY SERUM INJECTIONS.

BY LOUIS M. WARFIELD, M.D.,

Savannah, Ga.

The cases here reported were observed and treated by the writer in New York City during July and the first half of August, 1903. The object of the investigation was to study the cases of Shiga infection of the intestine in infants. It was the writer's duty to see cases in the tenements especially on the East Side and to use the serum as much as possible in those cases that were proven by bacteriological examination to be cases of Shiga infection. It was hoped that a large number of acute cases could be observed and followed by visiting the patients in their own homes. It was soon seen, however, that it was impossible to treat any considerable number of cases principally for the reason that there was comparatively little illness among the babies in the tenements. The cases that occurred were mostly of a mild type so that the withdrawal of the breast or cow's milk and a purge soon accomplished a cure. The very mild cases and a number almost moribund when first seen were not considered suitable for observation and so were not treated by serum injection. The cases were not taken in order but the severe ones alone were tabulated and as far as possible carefully followed. In all cases where the serum was used specimens of stools were examined by Drs. Gay and Stanton (see report). Much difficulty was experienced in getting fresh specimens for them as the cases were at times several miles from the laboratory. The various avenues for contamination of specimens and the long time frequently elapsing between the passing of the stool and the plating of it in the laboratory will account for the fact that many cases that appeared clinically to be typical infections with the bacillus of dysentery failed to show the specific organism and so were not available for record though treated with the serum.

Again it must be borne in mind that the difficulties of injecting the serum in suitable cases in the tenements were great; the apparent pain caused and the visible swelling produced by the injection of 10 or 20 c.c.

of fluid beneath the skin were in many cases too much for the mother's feelings and so one injection was often all that could be made.

The cases were treated in the usual manner, that is to say, nursing at the breast or cow's milk was discontinued and barley water substituted until the acute symptoms had subsided. Some purgative—castor oil or calomel was given. Occasionally bismuth or a chalk mixture was later administered. Other drugs were rarely used. A short history of each case follows:

Case I.—J. K., three and one-half months old; tenement-house patient. A Mongolian idiot, poorly nourished, had been bottle fed with grocery milk since birth. Duration of illness, four days; onset with vomiting and fever; twelve to fifteen loose, bloody, mucous stools a day; some tenesmus. There was marked anemia; sunken fontanel; cold extremities; some patches of broncho-pneumonia over both lungs behind. Temperature, 102°-104° F.; pulse, 140-160. He was given 8 c.c of "Harris" serum. No noticeable change in the number or character of the stools during the succeeding twenty-four hours. On the next day 5 c.c. of "Harris" serum was given. During the next twenty-four hours there were only three stools of the same character. The child's general condition was worse. Was again given 5 c.c. of the same serum. Death in twenty-four hours. The serum was given in this case to see if it could affect the existing intestinal infection and so possibly aid the child to recover from the broncho-pneumonia, which was the chief disease. The *Bacillus dysenteriæ* ("Flexner-Harris" type) was found in the stools.

Case II.—L. B., eight months old; tenement-house patient. Child breast fed and in addition was given grocery milk. Duration of the illness before observation, two days. Onset with vomiting, fifteen to twenty fluid stools, with mucus, no blood. General condition fair; surroundings filthy. Temperature, 101.8° F. Pulse, 128. He was given 10 c.c. of "Harris" serum. The next day there were eight stools, the character the same; temperature, 100° F. General condition unchanged. On the following day the temperature was 101.8° F.; pulse, 180. Five stools in the twenty-four hours, several of which contained blood. Was given 6 c.c. of "Harris" serum. after much persuasion. During the next twenty-four hours there were three stools, color watery green, much fecal matter and curds, some mucus, no blood. Mother was found on two successive visits nursing the child against advice. She took child to a doctor, who gave her some medicine and told her to feed the baby milk. The case was dismissed, as the mother refused to follow advice. The child undoubtedly improved under the serum, but it is impossible to say that all the improvement was due to the serum. The *Bacillus dysenteriæ* ("Flexner-Harris") was found in the stools.

Case III.—G. B., ten months old; Bellevue Hospital. Child was a foundling and no history could be obtained. When first seen the child was almost moribund; there was a film over the eyes; marked emaciation; retracted abdomen; the temperature was 100.2° F. Pulse not perceptible; breathing was labored. Was given digitalis and brandy, and 20 c.c. of "Harris" serum on July 22d, at 1:30 P.M. At 7:30 P.M. the condition seemed a trifle better, one stool fluid, brownish, foul, no mucus or blood; temperature, however, had risen to 104.8° F.

Twenty c.c. of "Harris" serum again injected. During the night the condition improved somewhat. Was sponged with alcohol, after which the child slept for nine hours, only being aroused to take albumen water, which he did well. The pulse became perceptible now and then, and it was possible to count it, Voided some urine. Two dark greenish and brownish stools were passed, containing mucus and blood. On July 23d the condition was distinctly improved. Temperature, 98.6° F. Pulse better, but still hard to count; extremities cold, but the circulation was slightly improved and child more quiet. At 11 A.M., 20 c.c. of "Harris" serum was given. At 6 P.M., conditions not so good. Temperature, 101° F. Pulse not good; breathing labored. No vomiting; three brown, watery stools in the last six hours; no mucus and no blood. At 7:45 P.M., 20 c.c. more of "Harris" serum given. Following morning was moribund, pulse imperceptible, profound toxemia; death at 5 A.M. *Bacillus dysenteriæ* ("Flexner-Harris" type) was isolated from the stools. In this case the injection of serum seemed to be followed by a decided but temporary improvement.

Case IV.—R. S., six months old; Bellevue Hospital. Duration of illness two days, and the onset was with vomiting and loose mucous and bloody stools, ten to fifteen in twenty-four hours, with some tenesmus. The general condition was good. He was given 10 c.c. of "Shiga" serum on admission, July 28th, at 5:30 P.M. The temperature at 9 P.M. was 102° F. Castor oil given. July 31st, August 1st, 4th and 5th he had 10 c.c. of "Shiga" serum. On August 6th, 11th, 12th, and 13th, he had 20 c.c. of "Shiga" serum. He did not improve.

At times he was bright, but relapsed into a whining, restless condition. The stools after the first injection were never more than six in twenty-four hours, but they occasionally were streaked with blood. His condition grew worse in spite of large and repeated doses of serum. He died a few days later. *Bacillus dysenteriæ* (true Shiga type) was found in the stools. At autopsy numerous follicular ulcers were found in the descending colon and sigmoid flexure and the mesenteric glands were swollen. There were also patches of bronchopneumonia in the lungs.

Case V.—M. D., ten months; Bellevue Hospital. No previous history could be obtained. Condition when seen on July 30th was good.

Stools were four a day, small, semi-solid, with mucus, no blood. Temperature 99° F. Was given 10 c.c. of "Harris" serum. For the next three days the stools were five to six a day, and some contained pus, no blood at any time. The condition remained good. She was given 20 c.c. of "Harris" serum on August 5th and again on the 6th. Stools were then four to five a day, no curds, no mucus, no pus, no blood. Child was doing very well and later was discharged cured.

B. dysenteriæ ("Flexner-Harris" type) was found in the stools.

Case VI.—B. F., eight months old; Bellevue Hospital; no history could be obtained. Was seen on July 30th. Stools were from three to eight in twenty-four hours, loose, contained mucus and at times blood. Temperature never exceeded 100° F. She had castor oil and colon irrigations and later bismuth. She did not do as well as expected and on August 4th she was given 15 c.c. of "Harris" serum. Again on the 15th she was given 20 c.c. of "Harris" serum and on the 17th 20 c.c. of "Shiga" serum. The stools after the last injection became better; they were four to six a day, containing some mucus but no

blood. The general condition improved very much and she was discharged on August 14th cured.

Bacillus dysenteriæ ("Flexner-Harris" type) was recovered from the stools.

Case VII.—A. C., two months old; Bellevue Hospital; no history could be obtained. The patient was extremely ill when admitted on August 6th. Some prostration and the extremities were cold. She was given castor oil and brandy. Stools were three to four a day, of foul odor, with mucus, no blood. On August 10th the child's condition was worse. The stools contained considerable blood. She was given 20 c.c. of "Shiga" serum at 2 P.M. and again at 6 P.M., but the patient did not rally. Coma set in and death shortly supervened. The temperature was subnormal. Dysentery bacilli of the "Flexner-Harris" type were found in the stools.

It will be seen that of these 7 cases 4 were fatal and 3 were cured or very much improved. Of the fatal cases 2 were practically moribund when first seen and the serum was given without the expectation of improving matters very much.

Case IV, although seen early in the attack and given serum at once, after apparently improving suffered a relapse and after daily serum injections amounting in all to 150 c.c., gradually sank and died. This was a case in which one might have expected a response to the serum.

The impression gained from the use of the serum was that in children, at least in these cases, it did not have a curative value. No ill effects of any kind were noted after the injections. As far as could be seen there was no rise or fall of temperature directly due to the serum or change in pulse rate except in the pulseless cases where brandy and other stimulants were also given. The injections also seemed to cause great pain which may have been due to the preservative but also to the distension of the tissues. The pain soon disappeared and the serum was in most cases rapidly absorbed leaving only a slight soreness on pressure for about 24 hours at the place of injection. No eruptions were noted in these cases and no infections were seen. The back was usually the spot selected for these injections. The amount varied from 10 c.c. to 150 c.c. Some cases were given 20 c.c. at a time but 10 c.c. was the amount usually used.

REPORT OF TWENTY-EIGHT CASES OF INFECTION WITH THE BACILLUS DYSENTERIAE IN INFANTS AND YOUNG CHILDREN.

BY ROBERT W. HASTINGS, M.D.,
Physician to the Boston Floating Hospital.

During the summer of 1903 there were observed twenty-eight cases of infection with the Bacillus dysenteriae in young children in the Boston Floating Hospital. Thirty-five cases in all were examined bacteriologically.

The Boston Floating Hospital received cases from dispensaries and hospitals and also those referred by private physicians. It is a boat fitted up with wards for permanent and transient cases and thus it was possible to keep patients under constant observation. In the permanent wards almost all the cases were severe ones. The cases making up this report were all observed in the permanent wards and hence the preponderance of what will be later described as the severe cases.

At first those stools containing blood and mucus were examined bacteriologically, later on account of stress of work only those from the severest cases. There was no examination of consecutive cases.

The bacteriological work was in charge of Mr. Arthur I. Kendall (see report). The patients were all from the tenement house class though many were not from the very poorest.

Thirty-five cases were carefully studied and in twenty-eight the presence of the Bacillus dysenteriae was demonstrated.

Negative Cases.

In three of the seven negative cases no cause could be assigned for the failure to find the bacillus dysenteriae. Two were evidently cases of meningitis probably tuberculous. One was a case of general miliary tuberculosis the tubercle bacilli being demonstrated in the stools. One was a case of typhoid fever and from the stools of the patient two years old the typhoid bacillus was cultivated.

Positive Cases.

Previous Attacks of Diarrhea.—The histories obtained were in many

instances unreliable. In four cases only was there a history of previous enteric disturbance. Of these cases three gave histories of previous attacks of diarrhea during the earlier summer. One case had had two previous attacks, one in the summer of 1902 and a second earlier in the season of 1903.

Character of the Food at Time of Attack.—Two were breast-fed exclusively; five cases were fed on condensed milk alone; three received ordinary table diet; cow's milk diluted with water or thin gruels without regard to accurate modification had been given to seven; proprietary foods alone had been given to three, in combination with milk to four; a restricted diet of bread, beef juice and milk had been given to three. In one case the diet was not stated.

Apparent Cause of Attack.—No one cause can be assigned to any case with a single exception. In most of the cases the food of the children lacked even ordinary care in its method of preparation. The milk was the usual milk of the household, in many instances kept in unhygienic surroundings. In no case had the food been sterilized before being given to the child. In one case, a breast-fed child, the onset seemed to be synchronous with the use of the breast pump.

Ages and Duration of Attack.—The average duration of symptoms before coming under observation was seven days. The longest period was six weeks.

The average period of observation was eighteen days. The shortest was in three patients who died on the day of entrance. The longest period of observation was sixty-three days. The average age was ten months, the youngest being three months and the oldest four years.

Character of Attacks.—Of the positive cases three are noted as mild, five as of moderate severity and twenty as severe. Those cases were considered mild whose temperature was 100.5° F. or lower, whose constitutional symptoms were very mild and whose stools were not more then ten a day the character of these being usually green with more or less mucus, rarely a little blood. The moderately severe cases had usually a temperature of over 100.5° F., more or less constitutional symptoms and stools with mucus and blood averaging ten or more a day. The severe cases were those with great prostration, usually but not always a high temperature and very numerous stools either mucous and bloody or very thin fluid. As mentioned above there was no consecutive examination of cases and only the severe ones or those having mucus and blood in the stools were studied bacteriologically. Of the mild cases two were discharged well and a third, entirely over the

enteric trouble, developed symptoms of what was probably central pneumonia from which she finally recovered.

Of the moderately severe cases one was discharged well, two were improved; one complicated by tuberculous adenitis and chronic otitis media was discharged unimproved and the remaining case developed lobar pneumonia from which she died.

Of the 20 severe cases there were 13 who died, 5 who recovered and 2 who were discharged improved, but ultimately died outside of the hospital.

Type of Organism.—Of the 28 cases, 23 were infected by the acid-producing or "Flexner-Harris" type of organism, 3 with the true Shiga type and in 2 cases both types were isolated. The small number of cases with the true Shiga type precludes much comparison. The 3 cases presented no marked differences from the rest of the cases. The 2 cases of double infection were both severe but had no essential differences in symptoms from the other cases. Of these 2 cases, one died and one recovered. Of the 3 cases of Shiga infection one was moderately severe and recovered, one moderately severe and improved and one severe case died.

Breast-fed.—Only 2 cases were breast-fed at the time of entrance. One, a boy eleven months old, well nourished entered with temperature 104.5° F., delirious, furred tongue, mild diarrhea, four to six stools per diem, green, with mucus. On heel of left foot a bleb surrounded by an erysipelatous process. Numerous abscesses of the leg developed later which were opened. The staphylococcus pyogenes aureus was isolated from these. There was final recovery. As the enteric disturbance was never severe and as a prolonged search of several hundred colonies revealed only one colony of the *Bacillus dysenteriæ* (Flexner-Harris) the relationship as a causative factor is problematical.

The other case was interesting as to etiology. The mother stated that on account of a cracked nipple she had begun a week previous to the onset to use a breast pump of which little care had been taken and the milk so obtained had been fed to the child. The child was a boy 10 months old, fairly nourished, somewhat rachitic, no teeth; stools 8 to 10 a day, green, with mucus and occasionally streaked with blood; considerable tenesmus. Temperature 99°—101° F. Child refused to nurse, feeding with dropper was resisted so as to exhaust child; after gavage he occasionally regurgitated. Vomiting was persistent and toward the end the vomitus contained traces of blood. On the day of death he had two convulsions.

Fatal Cases.—I.—Boy, seven months old. Well nourished, slightly anemic,

tongue dry, with white coating; in collapse on admission. Temperature, 104° F.; very weak; persistent vomiting; no tenesmus. Stools six to nine a day, green, with mucus and blood. Died five days after entrance in spite of stimulating treatment and the injection of "Harris" serum, 10 c.c., on each of three days. There was no change in the stools after this, the temperature rose to 105.4° and the child died.

II.—Boy, two months old, poorly nourished, slight rosary. Few râles at back; heart action weak; peripheral circulation sluggish. Child restless. Occasional vomiting. Stools six to ten a day, green, with mucus; some tenesmus. Treatment, stimulating and serum. Child lived nine days. The "Harris" serum was given six times, 10 c.c., on consecutive days. Child failed steadily. Stools unchanged.

III.—Girl, five months old, fairly nourished. Temperature, 102° to 105.6° F. Pulse weak; somewhat restless at times; prostrated on entrance, with marked vomiting. Lived forty-eight hours. Stools twelve, green, fluid, with mucus, and voided with severe tenesmus. Treatment, stimulating. No serum.

IV.—Girl, colored, three months, well nourished. Tongue coated; fontanel depressed; pulse weak, intermittent; extremities and skin cold and clammy; in stupor; temperature, 101.5° F. Stools twenty in one day, thin, faint green tinge. Face pinched. Died a few hours after entrance. Had two attacks of convulsions. *Autopsy.*—Slight hypostatic congestion of both lungs. Mucosa of colon slightly injected, no other gross evidences of disease.

V.—Girl, twenty months old; well nourished. Moribund on admission; prostrated; cyanosed and extremities cold; tenesmus; comatose. Temperature, 104.8° F. Lived two hours Treatment, "Harris" serum, 20 c.c. No response to saline infusion nor stimulation.

VI.—Girl, seven months old; well nourished. Prostrated; heart sounds weak; restless. Temperature, 101° to 104° F. Stools six to nine, green, with mucus and blood. Under observation five days. No response to any treatment. No serum.

VII.—Boy, thirteen months old; well nourished. Physical examination negative. Drowsy; slight tenesmus; stools five to ten a day, brown, with mucus. Constant vomiting. Temperature, 100° to 102.5° F. Lived six days. Treatment, 20 c.c. "Harris" serum, given once without effect. Stimulation of no effect. Died with meningeal symptoms.

VIII.—Girl, eighteen months old; well nourished. Prostrated. Temperature, 104.8° F. Tenesmus; stools four, yellow and green, with mucus. Lived twenty-eight hours after entrance. Treatment, stimulation. Autopsy showed an early stage of follicular ileo-colitis. No serum used.

IX.—Boy three years old. Poorly nourished. Physical examination negative. Drowsy; stools two to nine, green, with mucus and streaked with blood. Treatment: stimulation and saline infusion; no serum. Case moribund on entrance.

X.—Colored girl, four months old; fairly well nourished. Rachitic. Stools five to eight a day, greenish-yellow, with mucus. Dejections in several instances consisted of purulent material almost wholly small mononuclear lymphocytes. Suffered considerably from distension. The intestinal trouble had ceased when signs of pneumonia, followed by empyema and purulent pericarditis, appeared and from this she died. No serum had been used. Duration of illness fifty-five days.

XI.—Boy, five months old; well nourished. Restless. Stools two to four, greenish-yellow, with mucus, and passed with tenesmus. Gradually fell into stupor and died on the twelfth day. No serum used.

XII.—Girl, three months old; well nourished. Prostrated on entrance; somewhat restless; signs of pneumonia at right base, posteriorly. Autopsy showed broncho-pneumonia and the enteric tract normal. "Harris" serum, two doses, 20 c.c. each, without apparent effect.

XIII.—Boy, six months old; well nourished, slightly anemic. In poor condition on entrance; pulse weak, 134. Temperature, 103.5° F. Stools eight a day, green, with mucus. Under treatment eight days. "Harris" serum given twice, 10 c.c. No apparent effect.

XIV.—Boy, six months old; well nourished; restless. Marked tenesmus. Stools six to nine a day, much mucus and blood. In this case there were two distinct recrudescences. "Harris" serum was given for fifteen days in 10 c.c. doses twice a day for one week and later 20 c.c. twice a day for one week. The course of the case was progressively downward. The child developed purpura. Discharged after being under observation for six weeks. Child died a week later at the Children's Hospital.

Two cases were discharged improved. Both died later.

Serum Treatment.

Of the 16 who died 5 received serum in addition to all other treatment; of the 11 discharged well, 7 had serum; of the 4 improved 2 had serum; of the 4 unimproved all had serum before leaving the hospital.

Of the 5 who died and who received serum 1 received three doses of 10 c.c. each; one five doses of the same amount, and 3 received each one dose of 20 c.c.

Of those discharged unimproved 1 received two doses of 10 c.c.; 1 three doses and 1 eight doses of the same amount, while the fourth had 20 c.c. at one dose.

Of the cured who had serum, 3 had two doses of 10 c.c.; 1 three doses and one nine doses of the same amount, while 2 had the larger dose of 20 c.c.

One of the two discharged improved had a single dose of 10 c.c. and the other had five doses of the same quantity.

It does not seem that any positive conclusions can be drawn from our experience with the serum. We are confident that in no case was the child made worse by the injection.

A CLINICAL STUDY OF FORTY-FIVE CASES OF INFECTION WITH B. DYSENTERIAE (SHIGA) OCCURRING AT THE BABIES' HOSPITAL.

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At the Babies' Hospital, during the past year every child, passing mucus in its stools, has been carefully watched from a clinical standpoint, and if such stools persisted for any length of time, they have been examined bacteriologically to determine the presence of the *B. dysenteriæ* (Shiga). By this routine practice we have been able to recognize cases suffering from such an infection that would otherwise have been overlooked. A positive diagnosis has been made not only in cases presenting the features of a serious dysentery, but also in others where the disease had reached a subacute stage prior to admission to the hospital. The analysis of the symptoms presented by these cases forms the subject matter of this paper.

In collecting this material the stools from about 100 cases showing intestinal symptoms were examined. This laboratory work has been carried on by Dr. Martha Wollstein, Pathologist of the Babies' Hospital.

In 13 months there have been 45 cases in which the B. dysenteriae (Shiga) has been isolated from the stools during life. During this period 678 infants under 2 years of age have been treated in the hospital wards, and of these over half have been suffering from some form of gastro-intestinal disorder.

Nineteen cases in which this infection occurred were fatal. Twenty-six cases were discharged from the hospital, and in all but seven of these the intestinal symptoms had disappeared. Twenty-four of these cases were males, 21 were females. All but one were white children.

The greatest number of cases were observed in July, during which month, also, the greatest number of children were admitted to the hospital and the proportion of intestinal cases was highest.

7	cases	occurred in	March, 1903.
3	"	"	April, 1903.
2	"	"	June, 1903.
14	"	"	July, 1903.
6	"	"	August, 1903.
6	"	"	October, 1903
2	"	"	November, 1903.
1	"	"	December, 1903.
1	"	"	January, 1904.
3	"	"	March, 1904.

There did not seem to be any relation between the season and the severity of the attack. As large a proportion of severe cases occurred in the winter months as in the summer.

Table Showing Age, Result and Type of Infection.

Five were under 3 months of age; 3 died—1 severe, 2 mild; 2 recovered—both mild.

Fifteen were between 3 and 6 months of age; 7 died—1 severe, 2 moderate, 4 mild; 8 recovered—1 moderate, 7 mild.

Thirteen were between 6 and 9 months of age; 4 died—2 severe, 1 moderate, 1 mild; 9 recovered—3 moderate, 6 mild.

Five were between 9 and 12 months of age; 2 died—both severe; 3 recovered—1 severe, 2 moderate.

Five were between 1 and 2 years of age; 2 died—both severe; 3 recovered—2 severe, 1 mild.

Two were over 2 years of age; 1 died—severe; 1 recovered—mild.

From this table, it would seem that the age of the patient was an important factor in the result; ten of the 19 deaths occurring under 6 months of age; and 16 deaths of the total 19 under 1 year of age.

General Nutrition.—Much more important, however, in explaining the predominance of the deaths in the early months is the general condition of the child at the time of the attack. Most of the children of this series were from the New York tenements, and were in bad condition at the onset of the disease. The majority of the deaths occurred in the youngest infants and in those whose general nutrition was poorest.

Table of Age and Weight.

Five cases under 3 months old. Weights: 5¾, 6½, 7, 7, 8 lbs.

Fifteen cases between 3 and 6 months old. Weights: 6, 7½, 7¾, 8, 9, 9, 9¼, 10, 10½, 11¼, 11¼, 12, 12½, 14¾, 16 lbs.

Thirteen cases between 6 and 9 months old. Weights: 7½, 8½, 9, 9¾, 10, 10¼, 10½, 10½, 11¾, 12, 13½, 14¼, 15½ lbs.

Five cases between 9 and 12 months old. Weights: 8½, 11, 11½, 14, 18½ lbs.

Five cases between 1 and 2 years old. Weights: 14½, 16, 18¼, 18¼, 21 lbs.

Two cases over 2 years old. Weights: 16, 22½ lbs.

Type of Infection.—Of the 45 cases, in 12 the symptoms were those of a severe infection; in 9 it was only moderate. The number and character of stools, the amount of fever and the prostration, were considered as an index of the type of the infection.

In 24 cases the symptoms were very mild; there being practically no fever or prostration and the stools never being more than 6 or 8 in number, and though thin with more or less mucus, never containing blood.

Although, as we have seen, the prognosis is greatly modified by the age of the child and its general nutrition, it is not so easy to bring out the relation between the prognosis and the severity of the infection. Here we have also to consider the individual resistance of the living organism to disease. The prognosis is also affected by the presence of other disease. Thus in 22 of the 45 children, at the time of the discovery of the *B. dysenteriæ* in the dejecta, 8 were suffering from marasmus, 4 from bronchitis, 3 from broncho-penumonia, 2 from lobar pneumonia, 2 from acute gastritis, 1 from impetigo contagiosa, 1 from syphilis, and 1 from syphilis and nephritis.

Previous Diet.—Of the total number of cases, 25 had been fed cow's milk, 7 condensed milk, 6 were breast-fed and 2 were taking table food. The remaining 5 children had been fed cow's milk and different proprietary foods.

Of the 6 breast-fed cases, 2 were fatal; one was a twin 4 months old weighing only 6 pounds, who died in March with mild intestinal symptoms. The other was a terminal infection of moderate severity in a child 5 months old, weighing 12 pounds and suffering from hereditary syphilis. This child died in July. Two of the breast-fed children had severe infections in hot weather and recovered. Two breast-fed children, both well nourished, had mild infections in March and October, and both recovered.

With the exception of the breast-fed cases, most of the children had been badly fed, and all the proper rules in regard to the care of the food and general hygiene had been disregarded. All the children had been given unboiled water from the tap.

Previous Illness.—One case only of the entire series gave a definite history of severe diarrhea, which was three months before admission to the hospital. The second attack was, however, of moderate severity. In 2 cases pneumonia and in 1 case measles had directly preceded the dysentery. In 3 cases the stools were simply said to be "frequent" previous to admission. Four gave a history of mild diarrhea; and ten gave a history of severe diarrhea, *i.e.*, 7 to 12 stools in

twenty-four hours. There was a history of vomiting as well as diarrhea in 12 cases. In 1 case there was no history in regard to character and number of stools previous to admission and in 1 case the stools were stated to be normal.

Fifteen children were admitted with normal stools, and did not show any abnormal intestinal condition for from one week to two months after entrance. These children were brought to the hospital for other than intestinal ailments.

No definite information in any case could be obtained from the parents in regard to previous fever, prostration and other symptoms of interest.

Of those admitted with abnormal stools, there had been intestinal symptoms for:

3	days	or	less	in	7 cases.
5-7	"	"	"	"	6 "
2-3	weeks	"	"	"	8 "
4-5	"	"	"	"	3 "
"Always"		"	"	"	1 "
Not stated					5 "

Food During Attack.—While in the hospital, the food in 37 cases was never changed from the usual modified milk suited to the age and general condition of the child, as there did not seem to be enough symptoms of intestinal trouble to render a change of food necessary. The digestion of the upper bowel and the assimilation of food in many cases did not seem greatly impaired. The fact that two-thirds of these cases recovered may have been due in part to the fact that the digestion was not upset by change of food, and in this way the nutrition of the body lowered. In 8 cases the food was changed to broth, egg albumen or gruel in most instances because the intestinal symptoms were very severe. It seems from our experience that while a fluid diet was always indicated, that properly modified milk was contra-indicated chiefly in cases where there was gastritis or symptoms of involvement of the upper bowel.

Temperature.—In 21 cases of the series there was no rise of temperature over 100°; in 12 cases (all fatal) the fever ran from 100 to 106°; in 2 other cases, also fatal, there was pneumonia present which accounted for the temperature. In the 10 remaining cases there was a slight irregular rise in temperature, which in 6 cases was attributed to other diseases.

Character of Discharges.—Of the 45 cases, during the height of the disease:

11 had	less than 4-5	stools in	24	hours.
22 had	from 4-7	"	24	"
11 had	from 7-14	"	24	"
1 had	18	"	24	"

The stools in all cases contained mucus in varying amount; and in seventeen they contained blood. Eight cases showed blood in large amounts and once there was quite an abundant hemorrhage.

Under observation for dysentery:

1 day in 2 cases.
2-7 days in 6 cases.
1-2 weeks in 13 cases.
2-4 weeks in 13 cases.
1-2 months in 8 cases.
over 2 months in 3 cases.

Treatment.—As a routine all cases admitted during the summer months received a dose of castor oil. In 12 cases other purgatives were used. Except for the initial purgative, we did not find that drugs in any way modified the course of the disease, but often did harm in upsetting the stomach. Stimulants were employed, when indicated by the symptoms, whiskey, strychnia, and, occasionally, digitalis being used. Rectal irrigations of a hot saline solution were used in 5 cases, but except for the stimulating effect no benefit was observed.

Serum Treatment.—Anti-dysenteric serum was given in 14 different cases in 10 c.c. doses. Nine cases received only one dose; 3 cases, two doses; one case, three doses, and one case four doses. The doses were usually given on successive days.

Several times following the administration of the serum there was an apparent decrease in the number of stools and a change in their character for the next 24 or 48 hours. In no case were we convinced that the benefit was permanent. Urticaria twice followed the use of the serum. There were no untoward effects.

Fatal Cases.—As has been stated before, 19 of the 45 cases of infection with the B. dysenteriae died. In only 13 of the fatal cases, could the death be attributed to this infection. In 6 instances the dysentery infection occurred in children suffering from other diseases, and the intestinal symptoms had disappeared entirely before the end; the intestinal infection only influencing the result in weakening the resistance of the infant. Of the 13 deaths caused directly by the *B. dysenteriæ*, 8 children showed no other disease, and the infection in all these

was of a very severe type. In 5 of the 13 cases, the intestinal disease was a terminal infection in children suffering from other diseases; but, in only one of these was the infection of a severe character; 3 cases indeed exhibited the mildest symptoms, while one was of moderate severity.

In analyzing the 13 deaths due primarily to the dysentery bacillus, it is to be noted that 8 occurred in the summer months, 6 of these in July. The majority of the severe fatal cases developed in the hottest weather, as was to be expected.

Of the 13 fatal cases:

One was under 3 months old. Weight: 6 lbs.
Three were from 3-6 months old. Weight: 9, 12, 12½ lbs.
Four were from 6-9 months old. Weight: 7, 7½, 8, 10 lbs.
Two were from 9-12 months old. Weight: 11, 14 lbs.
Two were from 1-2 years old. Weight: 15, 16 lbs.
One was 2 years old. Weight: 16 lbs.

Again we find that age and general condition are the important factors in prognosis; 10 of the cases were under 12 months and all were poorly nourished. Only 3 cases with severe symptoms recovered; 2 of these were breast-fed and the weight and general condition of all three were far above the average for hospital patients.

Hospital Infection.—in 15 of the total number of cases, the intestinal symptoms appeared after the child had been in the hospital one week or longer. It seemed certain that the infection occurred in the hospital in at least 5 of these cases. For instance, a child two months old and breast-fed was admitted to the hospital for syphilis. It entered in December, and four months afterwards developed a mild form of dysentery. The stools had been normal before this attack. In such cases—in consideration of the age of the child on admission, the previous history, and the length of time under observation there seemed to be no doubt that the infection occurred in the hospital. The other cases could be ascribed to exacerbations of pre-existing infection, although in only one was there a definite history of previous diarrhea. If it is possible for such a contagion to spread in the hospital, where every care is taken to prevent such a misfortune, and where practically "typhoid isolation" is enforced, the danger must be much greater in a crowded tenement where the surroundings are unhygienic, and there is often gross neglect. In these cases of "hospital infection" the symptoms were very mild and the true nature of the disease might have escaped detection had not routine bacteriological examinations of stools containing mucus been made by Dr. Wollstein.

Lesions.—Seven cases in all came to autopsy. Of these 2 cases showed practically normal intestines. These children had mild infections from which they had recovered some weeks before death, which was due to other causes. The stools were normal before death and the *B. dysenteriæ* could not be found in post-mortem scrapings from the mucous membrane of the intestine.

In one case, that of an infant two months old, there had been a severe infection of several weeks' duration, which was the direct cause of death. The autopsy was made several days after death, and the post-mortem changes were so marked that nothing could be determined, except that there was no ulceration or necrosis of the intestine.

In 2 autopsies, the intestines showed only slight congestion and some enlargement of the solitary follicles. One of these was a colored child 14 months old, markedly rachitic, which had been sick one week with very severe intestinal symptoms. The death was apparently due to infection with *B. dysenteriæ*. The anatomical diagnosis, extreme rachitis and atelectasis, was made at the post-mortem. The second case was that of a child three months old, suffering from marasmus and broncho-pneumonia, where death was caused by a terminal infection with the dysentery bacillus, the symptoms being of the mildest character. The anatomical diagnosis, here, was broncho-pneumonia, general hyperplasia of the lymph nodes and fatty liver. In both of these cases *B. dysenteriae* (Flexner-Harris type) was isolated from the post-mortem intestinal scrapings.

In 2 cases only were the intestinal lesions of a serious nature. One of these a child 5 months old suffering with marasmus had died with a terminal dysentery infection. The intestinal symptoms, which had lasted about 2 weeks, were very mild, there was no fever and the stools were only slightly increased in number and contained mucus. The intestines showed small superficial ulcers throughout the small intestine. The Peyer's patches and solitary follicles of the colon were enlarged but not ulcerated. The intestinal coats were congested in patches. The mesenteric lymph nodes were somewhat enlarged. There was also pulmonary congestion and edema of the lungs and fatty liver. In this case, also, the *B. dysenteriae* (Flexner-Harris type) was isolated from the intestinal mucous membrane at autopsy.

The other case occurred in a child two years old, in wretched condition, weighing only 16 pounds, and just recovering from measles. The intestinal symptoms lasted altogether fifteen days and were most severe. The stools, which consisted of bloody mucus, were from 8 to 14 in twenty-four hours. There was also fever up to 102°, ex-

treme prostration and uncontrollable vomiting. Only a partial autopsy was permitted, the intestines alone being examined. The colon was mottled red and gray. The mucosa of the rectum and sigmoid flexure was covered with an adherent pseudo-membrane. In the colon between the patches of greenish membrane, were numerous, ulcers extending to the submucosa. The thickness of the colon wall was at least three times greater than normal. There were no ulcers in the small intestine; the lymph follicles were swollen, but only the Peyer's patch at the ileo-cecal valve was covered by pseudo-membrane. The appendix was slightly congested and covered with small superficial ulcers. The mesenteric glands were slightly enlarged and deeply congested. Almost pure cultures of B. dysenteriae (Shiga) were isolated from the intestinal scrapings.

In the cases coming to autopsy we find some discrepancy between the clinical picture and the pathological lesions, although in this last case the two fitted together very well. Possibly a larger series of post-mortem examinations may give more uniform results.

Remarks.—In the study of different features presented by this series of cases, it seems possible and even necessary for the sake of clearness to make several clinical divisions of the forms of intestinal infection due to the *B. dysenteriae*. It is of bacteriological interest to find this bacillus in the stools of sick children; but a few bad stools and the isolation of a micro-organism do not establish the existence of a distinct disease. The chief point of interest lies, then, in the question as to whether we have in children an acute intestinal infection with distinct and constant symptoms, comparable in any way with adult dysentery, and whether the cause of such an infection is a specific micro-organism. This series of cases is interesting in covering the experience of an entire year, embracing not only hot weather cases but infections occurring in the winter months.

In at least 12 of our cases we had to deal with acute intestinal infection, where in children previously considered well, there was a sudden rise in temperature from 100 to 106° accompanied by frequent intestinal discharges and considerable prostration. The stools ranged from 6 to 20 a day. They were always thin and contained mucus, and usually blood. The signs of general toxemia usually accompanied the intestinal symptoms. The fever, prostration, bad stools and toxic symptoms were present in all cases, but usually one of these prominent symptoms predominated. The disease ran a course of from one to three weeks, and, if terminating favorably, the recovery was gradual; the fever, number of stools, and general

symptoms subsiding together. In acute intestinal indigestion, which may present a somewhat similar picture, the disease is short and recovery often rapid. Three-fourths of these cases terminated fatally within ten days after the onset of the first symptoms. The results with a better class of patients would undoubtedly be less discouraging. However, the symptom-complex of an acute, grave intestinal disorder due to the *B. dysenteriae* seems established. In such cases we might claim that the clinical and bacteriological entity "infantile dysentery" had a right to recognition.

In a smaller number of cases where the intestinal infection has been superimposed on some other disease, we find a different clinical picture. Here the dysentery may be regarded as a terminal infection. There is no reason why, under such conditions, the intestinal symptoms should not be severe; in those observed they were always mild. Hence we speak of a mild infection proving fatal; as a child already enfeebled by disease cannot withstand what would otherwise be a slight diarrhea. In such cases there was seen an increase in the number of stools up to four or five a day, rarely more. The stools were thin and usually contained mucus, but rarely blood. Sometimes they varied but little from the normal. There was slight if any fever, no increase in the prostration, and no definite toxic symptoms. The infection proved fatal in a few days or a few weeks.

Of a similar type, were the inter-current infections seen in children suffering from other infections or constitutional diseases. For a period of 1 to 3 weeks the stools were more numerous, thin and contained mucus or even a little blood, but there was little or no fever or prostration. Such cases often recovered.

In about 9 cases, there was no preceding or accompanying disease and the symptoms were mild like those just described. In these children where the occasional bad stools were often the only clue to the disorder, the condition seemed to be more or less chronic. One such case was in the Hospital in March and again in July and the *B. dysenteriæ* was isolated from the stools on each admission. There was no history of diarrhea or of intestinal symptoms. This point is of interest in connection with the spreading of the disease by contagion. Some of these mild cases may have resulted from acute fulminating cases, such as described first, which did not go on to complete cure. No such mild case, unassociated with other disease, proved fatal while under observation.

Type of Organism.—The organism isolated from the stools in 44 cases was the "Flexner-Harris" type of the *B. dysenteriæ* and in one

case the true Shiga type of organism (not mannite-fermenting) was isolated. The two forms of the bacillus were never found together in one case, either during life or post-mortem. In 3 of the 7 autopsies made, the "Flexner-Harris" type of organism was recovered from the intestinal mucous membrane and in one case the true Shiga organism was isolated at post-mortem, it having been previously found in the stools during life. In one case no culture was made owing to the condition of the specimen, and in 2 cases the organism was not found, and in both of these cases, which were inter-current infections, the child died with normal stools several weeks after the dysentery infection.

Conclusions.—In general, from this study we believe that bloody mucus or much mucus in the stools, where there is no reason for such an appearance, as intussusception, extreme purgation, etc., indicates infection with the *B. dysenteriæ;* that even a little mucus points to such an infection, if such stools have persisted for a long time. In the last thirteen months' service at the Babies' Hospital the *B. dysenteriae* has been isolated from the stools of about one-half of the cases examined bacteriologically which exhibited symptoms of intestinal inflammation.

A certain number of cases of infantile diarrhea present a symptom-complex comparable to adult dysentery and are caused by the B. dysenteriae. To this disease the term "infantile dysentery" may be properly applied. In its severe form and in the class of patients which make up the inmates of hospitals and other institutions for infants, the disease has a high mortality.

Milder forms of intestinal inflammation may also be caused by the *B. dysenteriae.* While these are not usually serious, they may be so in very delicate children where as a terminal infection they may be the cause of death.

In general the prognosis varies with the age and general nutrition of the child.

Infantile dysentery is somewhat contagious. Even mild cases may cause a spread of the disease. Hence, disinfection of stools should be carefully practiced in every case.

CLINICAL CONCLUSIONS.

BY L. EMMETT HOLT, M.D.

Considerable new light has been thrown upon the subject of diarrheal diseases in infants and young children by the clinical investigations of the summer of 1903, although much still remains to be done. The summer was not a particularly fortunate one for such an investigation as it proved to be an unusually cool season, and the diarrheal diseases were neither so frequent nor so severe as in average years.

Several points are prominently brought out by all the clinical observations:

1. Infection with the *B. dysenteriæ* occurs under quite a wide variety of conditions. It is seen in breast-fed infants as well as in those artificially fed.

2. It occurs (*a*) as an acute primary infection in children previously well; (*b*) as a subacute infection without previous acute symptoms; (*c*) coincident with or following other acute diseases such as measles, pneumonia, etc.; (*d*) it is often seen as a terminal infection in children suffering from extreme malnutrition or marasmus.

3. It occurs as a mild intestinal disorder with few symptoms and these hardly more marked than those belonging to intestinal indigestion; also with local symptoms of considerable severity, yet with very little fever or constitutional depression; and finally, in its most severe form, with both local and constitutional symptoms of great severity.

4. It is not a disease of any one locality, having been seen with great and about equal frequency in all the large cities—New York, Boston, Philadelphia and Baltimore—where investigations were carried on; the only variation in type being that in the warmer cities the proportion of severe acute cases was rather larger. Nor is the disease one of tenements and hospitals, a number of the cases observed being in children living in the best surroundings, even in the country. In its prevalence, it appears to be as widespread as are summer diarrheal diseases.

Previous Diet.—The clinical reports include observations upon 237 cases. The previous diet was studied in most of these in the hope of gaining some information as to the mode of entrance of the organism into the body. Of the cases observed, 26 were previously breast-fed. While in most of these the infection was of a mild type, some were

severe and even fatal. That these attacks were, as a rule, milder than most of those seen, may be in part at least explained by the better physical condition, and consequently the greater resistance of the breast-fed infants. That so many attacks were seen in nursing infants, shows that we must seek for some other mode of entrance of the specific organisms than with the milk. Possibly it may be the water, although in this the dysentery bacillus has not yet been found. The practice of boiling water for the use of infants is seldom followed in the tenements, and water in some form was given to almost all the children. No special relation of the infection to any other food or any special kind of feeding could be discovered.

Relative Frequency.—The relative frequency of infection with the dysentery bacillus as compared with other diarrheal diseases of infancy, cannot be definitely stated from these reports. In only two groups of cases were systematic examinations made of consecutive cases. In the others, the cases for examination were more or less selected, and hence it is impossible to draw conclusions from them as to relative frequency. The two groups of consecutive cases were those from the Vanderbilt Clinic, a summer series reported by Howland and La Fétra, and those from the Babies' Hospital, a year-round series, reported by Reed. In the first group of cases the dysentery bacillus was found in 62 of 64 cases examined. They included every sort of intestinal disturbance attended by diarrhea. These figures, however, do not prove that in every instance this organism was the cause of the disturbance. In some of the cases the number of dysentery bacilli was apparently very small; sometimes only one or two colonies were discovered after a prolonged and careful search. But their presence even in such small numbers is interesting as showing possibly how mild attacks might develop into severe ones.

In this connection one should consider also Wollstein's observations upon the stools of normal children, a report of which follows: In this it appears that of the 32 infants whose stools were studied, in none was the dysentery bacillus found, while of 24 other infants dying from various diseases, not intestinal, where cultures were made from scrapings of the intestinal mucosa, in only 3 was the dysentery bacillus found, in 2 of which there were present evidences of catarrhal colitis, while the third gave a history of previous diarrhea.

In the Babies' Hospital series covering one year's service, about one-half of all the cases exhibiting clinical evidence of acute disorders of the intestinal tract, showed the dysentery bacillus. These figures indicate that this organism is a very important etiological factor, both in winter

and in summer; but that it is present in a much larger proportion of cases in summer than in winter.

Clinical Types.—Of the cases studied, 91 were classed as examples of severe infection. These were characterized by much mucus and generally blood in the stools, usually fever, but not always high, and by marked general prostration. There were 81 examples of moderately severe infection, in which there was much mucus and often blood in the stools, some fever but not much constitutional depression. There were 63 examples of mild infection, in which the constitutional symptoms were very few; blood was seldom present; there was little or no fever; but the stools almost always contained mucus. These figures indicate only that mild infections are very common; their relative frequency, however, is probably much greater than is stated here, since by several observers only severe cases were taken for examination.

The types of disease were essentially the same at all places where the observations were made. Infection with the dysentery bacillus was associated with almost every sort of intestinal disturbance accompanied by diarrhea, with, however, one notable exception, viz., the severe acute intestinal intoxication called "cholera infantum," with its sudden violent onset, protracted vomiting, high temperature, frequent serous discharges, great prostration, early collapse and often early death. There was only one case which at all approached this type, and this lacked some of the essential features. The infection with the *B. dysenteriæ* is associated rather with the inflammatory forms of diarrhea, and of all degrees of severity, the mildest and the most severe, the acute, the protracted and subacute; occurring both as a primary disease and a secondary disease, often occurring in institutions during the summer as a terminal infection in infants suffering from marasmus exactly as does broncho-pneumonia under similar circumstances in winter.

Up to the present time the organism has not been found in cases of chronic intestinal indigestion in infants and older children, even though mucus was present in the stools in considerable amount. In this series of cases there were observed no chronic cases such as have been described in adults where bacilli were found after many months. The cases of long duration which were studied in infants, were usually free from bacilli at the end, death being due to progressive marasmus.

The most characteristic clinical type and the one with which the organism was almost invariably found associated, was the acute febrile form with stools containing much mucus and usually streaked with blood. For these cases the term "infantile dysentery" would seem the

only proper appellation. This type seems so distinctive that we may safely regard it as a separate and distinct disease.

Types of Organism.—Of the 237 cases studied clinically, the "Flexner-Harris" or "acid" type of organism was present in 207, the true Shiga in 23 and both organisms were present in 7. No difference could be observed in the clinical manifestations in the different forms of infection. Furthermore, the relative frequency of the different types was nearly the same in all places where the observations were made.

Whatever may be said of the dysentery of adults, it would appear from these data that in infants and young children, in our large Eastern cities, it is the acid type of organism rather than the true Shiga with which we are chiefly concerned.

Mortality.—Of the 237 cases reported, 73 were fatal. This gives little idea of the gravity of the dysentery infection, since it is well known that the result in all forms of intestinal disease in infants depends upon nothing so much as upon the age and previous condition of the patients. Considerably more than half the total number, 139, were observed in hospitals. It was among these patients also that nearly all the deaths occurred, as might have been expected. The poor general condition of these patients and the late date of beginning treatment had most to do with determining the results. Again, in several it was noted that the patients recovered from the acute diarrhea but died subsequently from marasmus. Cases of this kind were seen in almost all the groups.

In all acute disorders of the intestinal tract complex conditions are present. No infection or intoxication can occur without producing marked functional derangement of digestion. In some cases the infection is slight, while the digestive disturbance is severe. The two bear a general but by no means a constant relation to each other. The child's symptoms may be due almost entirely to the indigestion and very little to the infection. These conditions stand in the way of success by serum treatment. While we may be able to combat the infection by the serum it may be without any power to improve the digestive disturbance. This also has a bearing upon the question of diet during the attacks.

Diet During the Attack.—The necessity of stopping milk during severe acute infections is universally agreed upon. There is, however, some difference of opinion in regard to the desirability of withholding milk from cases of moderate severity, without temperature, where the disease seems to be limited to the large intestine. In these cases the symptoms from which the child suffers are chiefly those of wasting

from chronic indigestion. There seems to be little doubt from the experience at the Babies' Hospital and Vanderbilt Clinic, that many of these cases do much better upon a properly modified milk than upon other substitutes employed, such as broth, barley water, albumin water, etc., with which the loss of weight is very rapid. In such cases the infection seems to play a minor part and the indigestion a major part, and therefore one should not have his attention too much upon the presence of infection but should manage the child's diet according to general principles as in other forms of intestinal indigestion. The mere presence of infection with the *B. dysenteriæ* therefore is in itself no reason for withholding milk, and its intelligent use seems to give much better results than the substitutes usually employed.

Prevention.—The fact that the dysentery infection is contagious seems to be established, but how and to what degree is not yet proven. In four instances, small ward epidemics were noted. From present experience a high degree of contagion does not seem probable. The spreading takes place most likely through the discharges. This calls attention to the necessity for disinfection and the closest attention to prevent contamination of food or water by persons handling the child's napkins. The rule followed in the Babies' Hospital is a good one for all institutions, viz., that the nurse who is in charge of the children's napkins shall not at the same time have anything to do with the food or the feeding.

SERUM TREATMENT.

In all there were 83 cases in which the anti-dysenteric serum was employed; 38 of these were fatal. On the whole the results were disappointing. No unfavorable symptoms followed its use in any case. In a few instances eruptions, usually urticaria, followed as occasionally after diphtheria antitoxin. In only 12 cases did a noteworthy improvement appear to follow its administration. A careful study of the cases in which the serum was used does not make the results quite as bad as at first appears. Too much evidently was expected. The physicians had in mind the striking effects seen after diphtheria antitoxin. These were observed in no instance, and it is doubtful if they ever will be. The conditions in the intestines are very complex and in no way comparable to those which are present in diphtheria. Great disturbances of digestion are in most cases present and the consequences of this remain long after a specific infection may have disappeared. Difficulties were found in the use of the serum. The quantity in the strength in which it was used was large. The mothers of dispensary patients would not allow its use except in severe cases, and

often would not return for a second dose. A brief summary of the cases seems desirable.

Freeman's Report.—Seven cases treated; all hospital patients; in two the attack followed measles, one child had diphtheria and pneumonia. In 4 cases no improvement. In 3 improvement apparently occurred, but 2 died later from marasmus long after the intestinal symptoms had disappeared. The only case which recovered was that of a nursing child. Full doses were given; all but one receiving from 5 to 10 doses of 10 c.c. each.

Howland and La Fétra's Report.—Ten cases treated; all dispensary patients. Serum used only in the severe cases. Two children received but a single dose; result unknown as they did not return; 2 died, one moribund when treatment was begun, the other recovered from diarrhea, but died long after from marasmus; 2 showed decided improvement after the serum. In the other 4, no apparent effects. Rarely more than 2 doses of 10 c.c. given.

Amberg's Report.—Ten cases treated; 2 hospital patients, 5 private practice, 3 not stated. Of the 5 severe cases, 3 ended fatally, 1 improved and 1 recovered; of the 6 moderately severe cases 5 recovered, 1 improved. Only one case received an injection on the first day and one on the second day; 3 had been sick four to six days and six more than one week. Six cases received two doses and four, five doses of 10 c.c. each.

Warfield's Report.—Seven cases treated; 2 observed in tenements, 5 hospital cases; 4 died. Two were moribund when the serum was given and one other had pneumonia; 3 apparently benefited by the serum. Two patients received but two doses, all the others received much larger quantities, one patient being given 150 c.c.

Hasting's Report.—Fourteen cases treated; all hospital patients. Serum was used only in the severe cases. Seven of these were fatal. Details of the fatal cases only are given; one of these was moribund at the time of the administration, one died in the seventh week of the disease; 5 were in poor condition at the time of the attack. No striking improvement seen in any case.

Knox's Report.—Twenty cases treated; of these 9 were fatal. Three cases apparently improved from the serum; in 17 apparently no improvement.

Cordes' Report.—One severe case seen late, no apparent effect.

Reed's Report.—Fourteen cases; all hospital patients; nearly all severe infections. Temporary improvement seen in several, permanent improvement in none. In 9 cases only one 10 c.c. dose was given.

Such in brief are the facts regarding the use of the serum in the 87 cases in which it was employed. That decided improvement appeared to follow its use in only 12 of the patients is not very encouraging. Several factors worked against success. In a large proportion of the cases it was used late in the disease. Again it was as a rule used only in the most severe cases; and, finally, at the beginning of the season no rules had been formulated as to the size and frequency of doses, hence it is evident that many of the doses were too small. Four patients were moribund at the time the serum was given. Of the 87 cases, 67 were hospital patients, and all familiar with hospitals for infants know the class of patients referred to.

The conditions of success, however, are, first, that it must be used early, before serious lesions have developed or before the patient's general nutrition has been too profoundly impaired. The latter refers particularly to cases in young infants. The second point is that experience shows that the serum must be used in repeated doses, one or two doses given each day and continued for several days if the attack is severe. I cannot myself feel from a study of these reports and from personal observation of some of these patients, that an adequate trial of the antidysenteric serum has yet been made. The favorable cases for its use are surely not the subacute infections, where the symptoms relate much more to the functional disturbance of digestion and the resulting impairment of the child's nutrition than to the specific toxemia of the dysentery bacillus; nor again can anything be expected from it in attacks which develop late in a condition of marasmus in hospital patients. The promising cases are rather the sharp acute attacks with symptoms of severe infection occurring in infants or older children with some powers of resistance; in other words, in patients where the real problem is to combat the infection, and not to maintain the nutrition of patients, which even before the infection was a matter of the greatest difficulty.

Inasmuch as at present nearly two days are required for a bacteriological diagnosis, and as the agglutination reaction is seldom present until the end of the first week of the disease, if used at all the serum must be injected on a clinical diagnosis. Its use would then be indicated in children taken with acute intestinal symptoms with blood and mucus in the stools, or with very much mucus in the stools with fever and symptoms of general infection. The serum surely must be used early and it must be given repeatedly, since what is desired is to stop a process and not to neutralize a toxin.

All rules as to dosage and frequency must at present be tentative.

From the experience of the past summer it would appear that a dose of at least 10 c.c. should be used daily in a moderate case; this being repeated two or three times daily in a severe case. Since we have no means of differentiating clinically the cases in which the infection is of the "Flexner-Harris" and of the true Shiga type, it would seem best at present either to use a serum from animals immunized against the two types of organism or that from animals immunized against the "Flexner-Harris" or acid type, since by far the largest number of cases are of this variety. Although the Shiga serum is not without some effect in infections with the "Flexner-Harris" type of organism, and *vice versa*, this effect is much less than with the serum obtained from inoculations with the specific organism concerned.

A much more extended trial and upon more carefully selected cases is necessary before definite statements can be made as to the value of the anti-dysenteric serum.

THE DYSENTERY BACILLUS IN RELATION TO THE NORMAL INTESTINES OF INFANTS.

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(From the Pathological Laboratory of the Babies' Hospital, May, 1904.)

Throughout this paper the term "Dysentery bacillus" is used to designate the bacillus described by Shiga in 1898 and isolated by him from cases of dysentery in Japan, by Kruse in Germany, by Müller in Austria and by Vedder and Duval in the United States, and also the bacillus found by Flexner in the Philippines in 1899, later by various observers in the United States (Duval and Bassett, in Baltimore, Park in Mt. Desert, Hiss, Collins, Goodwin and Wollstein in New York City), and by Jürgens in Germany in 1903. That both these organisms may be the cause of dysentery has been proven by the positive agglutination reactions with the blood of the patients from whom the bacilli were isolated. Shiga's bacillus does not ferment mannit; the "Flexner-Manila" bacillus ferments mannit with the production of acid. The agglutination reactions of these two types of Bacillus dysenteriæ are distinct, both with the blood of patients convalescent from dysentery and with the serum of animals immunized to one type or the other. Furthermore, according to Park and Collins,[1] the agglutination reactions serve to subdivide the second or mannit-fermenting type into three classes, of which one agrees with the bacillus isolated by Park in Mt. Desert, another with the "Harris" culture brought by Flexner from Manila, and a third found by Collins in New York City.

Whether the Shiga type of dysentery bacillus causes a more severe clinical type of dysentery and a more intense intestinal lesion than does the mannit-fermenting type of the bacillus, future observations must determine.

Shiga[1] makes the statement that the *B. dysenteriae* is never found in the dejections of healthy individuals nor of patients suffering from

[1]Trans. N. Y. Pathological Society, January, 1904.

diseases other than dysentery, and Flexner[2] was unable to demonstrate the organism "in healthy dejecta or in evacuations of persons (native Filipinos) suffering from beri-beri." Under Kruse's[3] direction, Stein examined the stools of thirty-three persons (presumably adults), and found that neither in health nor in diarrhea from various causes do (Kruse's) pseudo-dysentery bacilli occur in the feces. Drigalski[4] examined a long series of cases of simple intestinal catarrh with entirely negative results. Neither dysentery bacilli nor organisms resembling them were found. He is also emphatic in his statement that dysentery bacilli are not found in healthy subjects nor in connection with other diseases, but only in patients with dysentery. Knox[5] mentions the fact that Duval and Bassett examined the normal stools of twenty-five children, with negative results. Ford[6] records finding *B. pseudo-dysentericus* in intestinal contents examined in the course of his study on the "Classification and Distribution of Intestinal Bacteria in Man." Since, however, his material was obtained from autopsies "regardless of the morbid conditions present," these results can have no bearing upon the question as to whether or not dysentery bacilli which do or do not agglutinate with specific anti-dysenteric serum are present in the normal intestines. It is clear that the finding of Bacillus dysenteriae in a normal stool from a healthy individual cannot be looked upon as proof positive that the organism is a normal inhabitant of the intestinal tract, unless the previous history of the individual, as to exposure to dysentery infection and the presence of previous attacks of the disease, be positively known and such exposure excluded. While the bacilli are usually absent from the stools or present in very small numbers after the third week of an attack of dysentery, they may persist in the mucosa or sub-mucosa for a much longer time. According to Lentz[7] the dysentery bacillus seems occasionally to retain its viability for a very long time within the human body, as evidenced by cases in which relapses occurred many months after the primary attack of dysentery. Drigalski[8] reports such relapses as occurring from two to six months

[1]Centralbl. f. Bakt., Bd. 23, H. 14; Bd. 24, H. 22, 23, 24; Deut. Med. Wochens., 1901, No. 45.

[2]Middleton-Goldsmith Lecture, 1900. (Proc. N. Y. Path. Soc.)

[3]Deut. Aerzte Zeitung, 1902, No. 2.

[4]Veröff. a. d. Mil.-Sanitätswesen, H. 20, 1902.

[5]Journal of the Amer. Med. Assoc., July 12, 1903.

[6]Studies from the Royal Victoria Hospital, Montreal, Vol. 1, No. 5.

[7]Kolle & Wasserman, Handb. d. Pathog. Mikroorganismen, 1903, Vol. 2.

[8]Loc. cit.

after the original onset, in one case after the return of a soldier from China to his home in Germany. He looks upon these cases as exacerbations of an intestinal process which has remained without symptoms for a time (as is characteristic of chronic dysentery), rather than as a re-infection. It is conceivable that any mild intestinal irritation may dislodge the bacilli, with or without a return of dysenteric symptoms. Hence the necessity for knowing the history of all cases studied.

It is evident that positive proof as to the presence or absence of B. dysenteriæ in the normal intestinal contents of infants free from gastro-intestinal disturbance, whose histories can be traced from birth, must have an important bearing upon the question of the etiological relationship of B. dysenteriae to the diarrheas of infancy. For that reason the following study was undertaken[1] and conducted in two parts. First, children in the hospital wards, admitted for diseases other than digestive, were selected,—only those being chosen whose stools had been observed and found normal for some days. The bowels having been irrigated with saline solution (1—2 quarts), two drams of castor oil were administered one or two hours later.[2] In some cases citrate of magnesia in repeated doses was used instead of castor oil. All stools passed within the next ten hours were sent immediately to the laboratory. From twelve to thirty plates were poured from each stool, and eighteen to twenty-four hours later tubes of Hiss' semi-solid medium were inoculated from their colonies. All non-gas-producing bacilli were grown in litmus-milk, in glucose, lactose, saccharose and mannit broth in fermentation tubes, in mannit and maltose peptone agar prepared without meat, and on agar slants.

The number of children thus treated and examined was thirty. Two infants, admitted to the Hospital at the age of one and two days respectively, were not dosed with the laxative, but all their stools were examined during the time elapsing between their entrance and their death—three and two days respectively. Thus the stools from thirty-two infants with normal digestion were examined. In no instance was B. dysenteriae found.

The ages of the children ranged from one day to four years; six were under two months old, twenty-one under six months, twenty-eight

[1]The idea of examining the stools of an apparently healthy infant after the administration of a laxative was first suggested by Dr. Flexner last summer. Two children were then treated and studied, with negative results.

[2]I am greatly indebted to Dr. Dorothy Reed, House Physician at the Babies' Hospital, for the selection and treatment of these cases.

under one year, thirty-one under eighteen months, and one was four years old.

The diseases for which they were admitted were as follows:

Coryza	1
Ulcerative Stomatitis	1
Chronic Tonsillitis	1
Hernia of Umbilical Cord	1
Gastritis	3
Bronchitis	1
Furunculosis	2
Eczema	3
Rachitis	2
Chronic Meningitis	1
Tuberculous Hip Joint	1
Malnutrition	10
Gonorrheal Arthritis	1
Prematurity	1
Well babies	3
	32

Four died: from prematurity, chronic meningitis, marasmus, and hernia funiculi umbilicalis with localized peritonitis. In the last case only was an autopsy permitted, and the results of scraping the intestines, post mortem, are included in the second series.

Only one of these babies was exclusively breast-fed. The others were fed on milk mixtures, variously modified.

The stools, before the dosage, were noted as constipated or normal; never was diarrhea present. Following the lavage and laxative administration the stools varied in number from one to five. They were always yellow in color, thin fecal or formed in character, sometimes contained a few curds, and in fourteen instances the second or third one showed a small quantity of clear mucus. This was never excessive in amount, and no blood was present in any of them. The two youngest infants, one and two days old, passed meconium at first and later dark yellow feces.

Bacillus coli communis, B. lactis aerogenes, B. alcaligenes, Staphylococcus albus and Streptococci were found in varying numbers in these stools. But in no instance did any bacillus isolated from them suggest, by its biological characteristics, that it belonged to the group of B. dysenteriae (Shiga), nor did any one react with anti-dysenteric serum in dilutions higher than one to one hundred. Several times such reactions were obtained with colon bacilli.

The second part of the study included the examination of the scrap-

ings, at autopsy, from the mucous membrane of the intestinal tract in children who died of diseases other than intestinal. Twenty-four of these were studied, varying in age from one day to fourteen months, including one still-born infant and six under two weeks old from the Lying-In Hospital. These very young infants were entirely breast-fed. No case of dysentery was present in the hospital at the time that these cases were observed.

The technique was as follows: at the autopsy a portion of the jejunum, lower ileum—within six inches of the ileocecal valve—and rectum—about four inches from the anus—were tied off and then excised. Their surface was burned through, the opening enlarged with sterile scissors, and the exposed mucosa scraped deeply with a narrow platinum spatula. Suspensions in neutral broth were made from these scrapings, and the plates poured from them at once. The aim was to obtain that portion of the intestinal contents adherent to the mucosa, rather than the feces free in the lumen. From thirty to thirty-five plates were poured from each case: 10-12 from the rectum, the same number from the ileum, and 6-10 from the jejunum.

The clinical diagnoses in these twenty-four cases were as follows:

Septicemia	1
Prematurity	2
Umbilical cord hernia	1
Pyemia	1
Broncho-pneumonia	4
Post-diphtheritic paralysis	1
Marasmus	8
Congenital syphilis	1
Cerebral Hemorrhage	1
Atelectasis	3
Stillborn from cord compression	1
	24

The histories state that the stools were normal or constipated in twenty cases. In one (congenital syphilis) the stools were green and mucous occasionally, but normal for the most part. The other three cases are to be detailed later.

The intestines at the autopsy were found to be normal in seventeen instances. In two a catarrhal colitis was present, the mucosa of the colon being congested and covered with a comparatively large amount of grayish-white mucus, while the solitary follicles were distinctly enlarged, but in no instance ulcerated. These changes were most marked in the rectum and sigmoid flexure, least marked in the transverse and descending colon, and fairly severe in the cecum.

On microscopic examination the superficial epithelium was found to be lost; the glands showed many "goblet" cells among their lining epithelium, a mass of mucus and granular débris lay upon the free surface of the glands in some places, the blood vessels of all the coats were congested, and the solitary follicles showed a simple hyperplasia. No loss of substance below the lining epithelium had occurred. The sub-mucosa was somewhat edematous, but no cellular infiltration was present in this or in the muscular coats.

In another case the solitary follicles in the colon and the Peyer's patches in the ileum were all swollen and congested. No ulceration was present, and no increase in the amount of mucus was noted. Finally the solitary follicles in the colon were very slightly enlarged in three cases, without any other change.

Twenty-one cases were entirely negative for B. dysenteriae. In three it was present, once from the ileum and rectum, twice from the rectum only. The histories of these three cases follow briefly:

(1) F., female, three months old. Good family history. Nursed two weeks. Vomited all foods tried. Stools "bad." Small emaciated child; lungs negative; abdomen flat. Weight, 4 pounds 12½ ounces. After admission she vomited food and curds frequently. The stools were green with a little mucus at first, but after four days became smooth and normal. She died one month after admission. At autopsy the ileum and colon were deeply congested and the solitary follicles and Peyer's patches swollen but not ulcerated.

(2) C., male, three months old, had cleft palate. Never nursed. Fed store milk, and regurgitated through the nose after each feeding. Did not gain in weight. Small, poorly nourished child. Heart and lungs clear. No vomiting; normal stools. Weight 7 pounds 4 ounces. In three weeks he gained one ounce. Five days before death the stools became frequent—five in twenty-four hours; green, with curds and mucus. The temperature never rose above 101.8° F. Died one month after admission. At autopsy, catarrhal colitis.

(3) H., female, three months old. Was premature (seven months), kept in an incubator two months and nursed. She vomited a little and stools were green since. In the hospital less than two days. Vomited curds. Stools green and smooth, four in number. At autopsy, catarrhal colitis.

It is evident that these three infants cannot be included under the head of "normal children" as far as their gastro-intestinal history is concerned, although their digestive disturbances by no means dominated the clinical picture, and they were in no sense ill with dysentery. One of them had normal stools at the time of her death. They emphasize very strongly the fact that, unless a child's history is known from birth, the finding of the dysentery bacillus in an apparently normal stool can be misleading in its significance.

The fact that two of these three positive cases are the only ones in which an inflammatory intestinal lesion was found, is of interest in this connection. In the case C., the dysentery infection was a terminal one occurring about five days before death. (One positive dysentery case was in the hospital at the time.)

Case H. was in the hospital but thirty-six hours before her death, had had green and frequent stools for one month before admission, and probably entered the hospital with a dysenteric infection of a mild degree. This seems a more rational explanation than the assumption that she acquired the infection during her short stay in the hospital, when no other positive case was present in her ward.

F. had had "bad" stools for two months before admission, but had recovered from them; and throughout three weeks of her stay the stools numbered from one to three daily, and were well digested and smooth. This was probably one of the cases in which the bacilli remained latent in the intestinal mucosa after recovery from an attack of dysenteric infection.

Bacteriological examination: Case F.—In the plates poured from the rectal scrapings, two non-gas-producing organisms were found to be non-motile bacilli which grew in the fermentation tubes without forming gas, in glucose, saccharose, lactose or mannit broth. Litmus-milk became slightly pink in twenty-four hours, but never coagulated; the blue color (like control) was restored on the fourth day. Acid was produced in mannit, maltose, dextrine and lactose peptone agar made without meat. Saccharose remained unchanged. The agglutination reactions were slow in appearance. Thus in two hours, in dilutions of 1-50, agglutination began, and in sixteen to twenty hours it was complete in dilutions of 1-1000; negative in 1-1500. For the serum with which the agglutination reactions were made I am indebted to Dr. Park. It is that of a horse immunized with mixed cultures of the Shiga, the Flexner-Manila and the New York City (type A, mannit-fermenting) dysentery bacilli.

Five c.c. of a forty-eight-hour bouillon culture injected into the peritoneal cavity of a medium-sized guinea-pig resulted in death within twenty-four hours. From the bloody serum in the peritoneal cavity the bacillus was recovered in pure culture.

A rabbit treated with dead cultures has now reached the point where its serum reacts to the bacillus in dilutions of 1-2000, having been negative in 1-10 before the injections began. The Shiga type of B. dysenteriæ fails to react with the rabbit's serum in dilutions of

1-10. Dysentery bacilli of the *mannit-fermenting type A* of Dr. Park (isolated from a Foundling Hospital case) reacts as high as 1-500.

These experiments are still being carried on.

Case C. From the ileum plates three non-gas-forming organisms were obtained, and two from the rectum. These had the cultural characteristics of Case F., but the agglutination reaction is much more rapid in appearance and is positive in dilutions of 1 to 1500, thus approaching very closely the control *mannit-fermenting type A* which was used throughout and which reacted in dilutions of 1-2000 with the serum obtained from Dr. Park (Horse 221).

Case H. Four tubes of mannit-fermenting B. dysenteriæ were isolated from the rectum only. They grew and reacted like the bacillus isolated from Case C.

Using this mixed serum from the Board of Health (Horse 221 immunized with the Shiga and mannit-fermenting type A bacilli), absorption experiments were made according to the technique of Dr. Park.[1]

The results are given in the following table:

Types.	Control Absorption with			Type A.	Type B.
		H.	C.		
Shiga	+500	+150	+150	+150	+250
A. Flexner B.	+1,500	—10	—10	—10	+400
New York City	+1,500	—10	—10	—10	+400
B. New York City	+700	—10	—10	—10	—10
F.	+1,000	+50	+50	+50	+100
H.	+1,500	—10	—10	—10	—10
C.	+1,500	—10	—10	—10	—10

H. and C., therefore, apparently belonging to the mannit-fermenting type A of dysentery bacilli; that is, their specific agglutinins are similar to those possessed by the "Flexner-Harris" type, in contradistinction to those of the Mt. Desert type.

The bacillus from Case F. differs from either of the above types, and *may* be found, on further study, to fit in with Dr. Park's type C.

From this study the following conclusions may be drawn:

In the normal stools of young infants during life, and in the upper layers of the normal intestinal mucosa at autopsy, B. dysenteriæ is not present.

[1]Proc. of the N. Y. Patholog. Soc., January, 1904.

The accompanying table gives the facts about the twenty-four cases examined at autopsy:

No.	Age.	Clinical Diagnosis.	Character of Stools.	Intestines at Autopsy.	Bacteriology.
1	Stillborn	Cord about neck		Normal. Meconium in colon	Jejunum, ileum and sigmoid sterile
2	1 day	Atelectasis	Meconium	Moderate congestion of coats of colon	Gas-producing bacilli only
3	2 days	Cerebral hemorrhage	Meconium	Normal	Gas-producing bacilli only
4	3 days	Prematurity	Meconium	Normal	Gas-producing bacilli and cocci
5	4 days	Hernia of umbilical cord	Meconium and yellow feces	Normal	Gas-producing bacilli and cocci
6	9 days	Atelectasis	Normal	Normal	Gas-producing bacilli only
7	11 days	Septicemia (from pus cord)	Normal	Slight swelling of sol. follicles in colon	Gas-producing bacilli and cocci
8	11 days	Atelectasis	Normal	Slight swelling of sol. follicles in colon	Gas-producing bacilli only
9	2 weeks	Prematurity	Normal	Normal	Gas-producing bacilli only
10	17 days	Marasmus	Normal	Normal	Gas-producing bacilli only
11	1 month	Syphilis	Green and mucus alternating with normal	Normal	Gas-producing bacilli and cocci
12	32 days	Marasmus	Normal	Normal	Gas-producing bacilli only
13	2 months	Marasmus	Normal	Normal	Gas-producing bacilli only
14	2 months	Broncho-pneumonia	(Only one day in hospital. None observed,	Normal	Gas-producing bacilli only
15	2 months	Broncho-pneumonia	Normal	Normal	Gas-producing bacilli only
16	2 months	Marasmus	Normal	Normal	Gas-producing bacilli only
17	3 months	Marasmus	Green with mucus alt. with normal	Congestion of ileum and colon; swelling of P. p. and sol. fol.	B. dysenteriæ in rectum
18	3 months	Marasmus and cleft palate	Green with mucus. 5 in 24 hours	Catarrhal colitis	B. dysenteriæ in ileum and rectum
19	3 months	Marasmus and prematurity	Green, undigested	Catarrhal colitis	B. dysenteriæ in rectum
20	6 months	Broncho-pneumonia, otitis	Constipated	Normal	Gas-producing bacilli only
21	8 months	Marasmus	Yellow and thin	Sol. fol. in colon slightly swollen	Gas-producing bacilli only
22	8 months	Broncho-pneumonia and perinephritic abscess	Normal	Normal	Gas-producing bacilli only
23	11 months	Pyemia	Constipated	Normal	Gas-producing bacilli, many cocci, and B. alcaligenes
24	14 months	Post-diph. paralysis	Normal	Normal	Gas-producing bacill and cocci

B. dysenteriæ may be present in the intestinal mucosa in cases of a very mild catarrhal inflammation of the colon, either as a terminal infection or as the remains of a previously active infection, when the clinical manifestations do not warrant the diagnosis of dysentery.

An infant's previous history is indispensable in judging of the significance of the presence of B. dysenteriæ in the stool or the scrapings from an apparently normal case.